THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 147, NO. 8 — CHICAGO, ILLINOIS — OCTOBER 20, 1951

COPYRIGHT, 1951, BY AMERICAN MEDICAL ASSOCIATION

GENERAL PRACTICE OF RADIOLOGY

CHAIRMAN'S ADDRESS

Joshua C. Dickinson, M.D., Tampa, Fla.

One naturally thinks of radiology in terms of diagnosis and therapy, and a division of the specialty on this basis has been strongly urged by some radiologists. I think of radiology as divided also into private and institutional practice. Since I have devoted my efforts to the private practice of clinical radiology in my own private office for more than 30 years, obviously my reasoning is influenced by my experience. It is from this point of view that I shall discuss some of the problems of general radiology.

In institutional work, particularly in large hospitals and teaching institutions, patients are seen by a group of specialists in various fields, and the problems of the consultant in radiology are altogether different from those presented to the radiologist in private practice. The latter sees the patient not infrequently on receiving a note or telephone call with the request, "Please see what you can do to find out what is the matter with this patient."

FUNCTIONS AND OBLIGATIONS

The foregoing statement is not a reflection on the general practitioner, who refers most of the patients. His is a perfectly legitimate request, and a recognition of the radiologist as a consultant in the fullest sense rather than as a specialist whose practice is limited to a narrow field. The obligation of the radiologist is to do exactly what has been requested, and that is to try in every way at his disposal to be of constructive help in the handling of a given problem. To render this aid the radiologist must be sufficiently interested and have sufficient time to take the history, make a physical examination, and display a real interest in the patient and the problem presented. If the examination is carried out in that way, the patient knows he has seen a doctor and will know the doctor's name, information of which he is commonly unaware when he is seen in institutions. Frequently, the patient who has been examined in a large institution knows the name of every consultant except the radiologist; he knows only that he has been sent to the x-ray department.

DIVISION INTO DIAGNOSTIC ROENTGENOLOGY AND THERAPEUTIC RADIOLOGY

Certain radiologists have insisted on the importance of dividing radiology into diagnostic roentgenology and therapeutic radiology. In the main, this division has been urged by those practicing therapeutic radiology in large institutions. Those of us who practice general radiology are referred to, in a not too complimentary manner, as "general practitioners of radiology." That certain radiologists, because of circumstances or personal interest, will devote their time to one or the other of these fields is, of course, to be expected. This is as it should be, just as certain radiologists will devote their energy to certain restricted fields in diagnostic roentgenology. I cannot, however, believe that in the foreseeable future this division is feasible in the average community. In this country the geography and the distribution of population do not lend themselves to this arrangement. Only a small percentage of the population can be seen by the most expert.

I am far more interested in the competency of the average general radiologist that in that of the "specialized" specialist whose field of knowledge is becoming more and more restricted. The large hospitals and medical centers will, as a result of special interest and circumstances, develop men specially competent in therapeutic radiology, even in special fields of this therapy, as well as in diagnostic roentgenology and its special fields of diagnosis. I believe that radiology will contribute more to medicine and be of greater service by the continuation of the practice of general radiology than by a division of the specialty into separate fields of diagnosis and therapy. I have heard the remark that "diagnostic roentgenology has little of the art of medicine; this is only for the therapist." I agree that this observation is true as diagnostic roentgenology is practiced by some radiologists, but it is not true if it is practiced as it should be and if the radiologist is to be looked up to with the respect accorded a consultant in the true sense.

Read before the Section on Radiology at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

RESIDENT TRAINING

I have attended a number of teaching conferences sponsored by the American College of Radiology and also have listened to a number of symposia before the special societies on residency training. In the teachers' conferences on undergraduate training the argument is usually stressed that not enough of the students' time is available for undergraduate training in radiology. With every other specialty it is the same. The deans of the medical departments are fully conscious that there are only so many hours available and wisely, I believe, take the position that their first obligation is to furnish the student with a broad basic training in general medicine. The modern medical curriculum does not allow time for training specialists. In the various symposia on graduate training, usually participated in by a diagnostician, a therapist, a pathologist, and a physicist, each thinks that too little time is given to his particular branch and that the other branches are overemphasized.

All too often in these symposia there is little mention of the training of better doctors. The residents in radiology attend clinical conferences and meet other requirements, but do they get into wards, actually see patients, and have an opportunity to get the patient point of view? We must not lose sight of the fact that, they, the patients, are interested parties. It seems to me that frequently this all-important part of training is neglected in the desire to turn out doctors highly trained in the science of radiology. Do not misunderstand me: I am convinced that the end is being attained in this respect. I am equally sure that in many cases the trainees are undertrained in the art of clinical medicine. I believe that one year of general internship is a totally inadequate basic training to fit a young physician to enter a special field and fulfil the qualifications of a consultant in that field. In fact, I seriously doubt if the average young physician has been exposed to enough general medicine at the end of one year to know what he wants to do in the special fields. It is my opinion that a decision arrived at after one year's internship is more apt to be based on personal admiration of a chief in a department, or the belief that the monetary returns are better than the average or the hours more satisfactory, or on something other than a real interest in a particular field. I believe it to be far more important that after a quarter of a century of professional life a practitioner of medicine be able to say that he has enjoyed the work in his particular field more than anything else that he might have done. Obviously, such a declaration is much more likely to be made if the decision is reached after the individual trainee has had sufficient opportunity to find out what his real interests are.

PRIVATE PRACTICE OF MEDICINE VERSUS HOSPITALS

The practice of radiology will be best safeguarded in the future if radiologists conduct their practice in private offices rather than move it into a hospital. I know it is much easier for a young radiologist to begin his practice in an already equipped department in a hospital. I also know that he will never have the same sense of security in any hospital that he can have in his own private office. I can see no reason why the practice of radiology cannot be carried out in a private office just as is done in other fields of medicine. Certainly the vast majority of patients are ambulatory, and I think most of them prefer to be seen in a private office rather than a hospital.

There are certain fields of diagnostic roentgenology and certain phases of irradiation therapy that are distinctly hospital procedures, but in the main radiology can be practiced just as satisfactorily, if not more so, in private offices. The physician-patient relationship can be maintained in a private office. The patient knows that he is seeing a medical consultant and not being examined in some hospital department, where all too often he does not see or know the consultant who is responsible for the examination and for whose services he pays a professional fee. The practice of radiology in hospitals should be limited to hospitalized patients, and I can see no insurmountable reason why the department of radiology should not be conducted on the same basis as the department of surgery. I realize that it means a division of fees into the technical and the professional, and I also know that this thought is the rankest heresy to most radiologists.

Most of the economic differences that have arisen between hospitals and radiologists are basically due to the fact that the relation of the radiologist to the hospital has differed from the relationship of the other members of the staff. Radiologists have insisted that they want the same relationship as the other members of the staff, but when the chips are down, do they? To me the encroachment of the hospital in the field of the practice of medicine is more of a real threat to the radiology of the future and to all medicine than any plan of compulsory health insurance yet proposed.

V 147
1951

THE AMERICAN BOARD OF RADIOLOGY

I regard the American Board of Radiology, together with the other specialty boards, as the most progressive step in medicine in my lifetime. Through these boards there have been set up certain minimal qualifications that a physician must fulfil before he will be given a certificate of competency in any special branch of medicine. Fundamentally, this requirement is of prime importance to the patient and safeguards his best interest. I think, however, that a false evaluation is commonly placed on the fact that a physician is a diplomate of one of the specialty boards. Too often the newly certified diplomate is looked on as a fully competent consultant in a specialty, whereas it only means that he has fulfilled certain basic requirements in training and has passed certain examinations satisfactorily. He is merely qualified to go out and learn to practice his specialty as it applies to the general field of medicine. His position with regard to his specialty is analogous to that of the graduate in medicine who has received his M.D. degree and has served an internship.

Residency training is not supposed to turn out finished specialists; in fact, a state of perfection is never reached. Certainly the sum total of one's knowledge is added to constantly by further study and experience. Yet all too

often the recent diplomate who has just finished his residency takes over as head of the department of a large hospital, the principal consideration being that he is a diplomate of the American Board of Radiology plus the fact that a financial arrangement can be made which is to the advantage of the institution. This placing of boys in men's places is regrettable and is an exploitation of the patient who is referred to that department. It is detrimental to the best interest of the patient, to the radiologist, and to the entire field of medicine. I think that the Board of Radiology should certify applicants in the general field of radiology and that the issuing of limited certificates in the various fields of the specialty is a mistake. Every diplomate should have a sound basic training in general radiology, and then, if because of circumstances or special interest he devotes his time to a limited field in therapy or diagnosis, he will be all the better qualified because of the general training.

THE FUTURE OF RADIOLOGY

The future of radiology will be what we radiologists make it. Will we be wise enough to curb the trend toward overspecialization within our ranks? If we are real clinicians and if we practice our specialty better than anyone else can practice it, we do not need to fear that diagnostic roentgenology will be taken over and divided among the various specialties. If, on the other hand, we turn our patients over to the technician, if we are too busy to see patients and maintain the proper patient-physician relationship, if we continue to move our private practice into hospitals where we are subject to every whim and dictate of the hospital administration and boards of directors, then radiology, in my opinion, will cease to be an attractive field that will attract well-trained capable physicians who are interested in clinical medicine.

603 Citizens Bldg.

RESPONSIBILITY OF PHYSICIAN TO PATIENT

Russell S. Boles, M.D., Philadelphia

Medicine has reached the crossroads. Either it must pursue the upward hard road of individualism, gathering unto itself more laurels and further glory, or descend the soft road of regimentation and subsidization—with all its pitfalls—to a level of mediocrity and imperfection that will cost it much in the esteem and reverence it has so long enjoyed. There is no group of persons in this country who have a grander opportunity than the physicians for assuming leadership in directing the course humanity will take today. Health and disease dictate the destiny of nations as well as individual persons—and indeed of whole civilizations—as history will show. Who then is better suited to sit in the council of those who would save the world than the physicians.

A multitude of duties and responsibilities impose themselves upon the physician. He is supposed to be an authority not only in matters pertaining to health but likewise to those of a personal, social, and civic nature. He is not endowed by virtue of education or native attributes with any more of the facilities of life than are his colleagues in other professions, yet he is regarded as a minister of faith as well as healing and as counselor as well as king by the hosts of friends and patients he acquires through the years. Such is the unique and honorable status of the physician, particularly of him who is in general practice. Who of us can deny that the attainment of such distinction is the measure of real success. It is a reward that is enduring and wholly satisfying, and who of us does not aspire to it beyond material things. Certain am I that reward of such character is the hope and ambition of every young man and woman who undertakes the study of medicine—though they may not always be aware of it. With this as the horizon of the physician—a man of good conscience, as the great majority of them are—what a staggering responsibility he must assume.

Robert Louis Stevenson described an army, though he did not call it such, that without sword or gun could win any war in history if it would only muster its courage, endure its disciplines, and exhibit the virtues it has always been wont to have. I refer to the army of physicians. In his dedication to "Underwoods," that volume of exquisite poems of nature, Stevenson pays tribute to such an army in the following words:

> There are men and classes of men that stand above the common herd; the soldier, the sailor, and the shepherd not infrequently; the artist rarely; rarelier still, the clergyman; the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with, and only remembered to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race. Generosity he has, such as is possible to those who practice an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Heraclean cheerfulness and courage. So it is that he brings air and cheer into the sickroom, and often enough, though not so often as he wishes, brings healing.

How may the medical profession live up to such a tribute? Obviously, first, by the selection of young men and women who show evidence in their background, personality, and capacity for assuming responsibility and leadership that they are suited to the profession. In my humble opinion this will not be accomplished by medical aptitude tests. With all due respect to the eminent specialists in their respective fields, I would ask by what measure is an English professor, a mathematician, a sociologist, and a physical chemist suited to prophesy whether a young man's professional success in handling sick people is in any manner whatsoever dependent on his ability to answer the following sample questions taken from an editorial in the *New England Journal of Medicine:*

> A sodium atom and a sodium ion (*a*) contain the same number of electrons; (*b*) have identical nuclei; (*c*) are isotopes; (*d*) have the same physical properties; or (*e*) differ in the number of protons they contain. Divide 4.80×10^{10} by 5.27×10^{17}.

Read before the Section on General Practice at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

In all the history of medicine one must wonder how many great clinicians of the past ever would have answered such questions. What a shocking catastrophe it might have been had they been subjected to such a thing. And how shocking it might be today if we knew how many fine able young men never gain an opportunity to satisfy the longing in their hearts to practice medicine because they did not show a proper aptitude rating.

Dr. Willard C. Rappleye, Dean of the Faculty of Medicine at Columbia, has aptly said,

> There is no such thing as "premedical" education, nor should students in colleges who plan to enter professional schools be regarded as premedical or predental students. The college preparation for medical, dental, and public health fields should not be professional in character. So-called premedical education should be abolished in the colleges of the country.

Dr. Rappleye contends that undergraduate institutions should try to give the students as broad a cultural background as possible. Training on the college level, he declares, "should be a preparation not for medicine or dentistry or public health, but for life." Consistent with Dr. Rappleye's contention, it is evident that attempts are being made to select students for medicine who are fitted for the profession by their human qualities as well as by their intellectual attainments. High academic standing may indicate a student is likely to succeed in a technological field, though even here it is being shown that he is the better, who possesses a cultural education. It has been well shown that academic standing does not necessarily indicate that an individual will become a good physician; as a matter of fact, when he lacks appropriate personal qualities and training he is likely to fail as such, despite his intellectual abilities. Much light, no doubt, will be thrown on this whole matter by the report of the subcommittee on Professional Education of the Survey of Medical Education. The organization and objectives of this committee as outlined recently by its chairman, Aura E. Severinghaus, satisfy an urgent need.

The properly selected student can become a great asset to the medical profession. This will be achieved, however, only by giving him full opportunity for developing his native attributes. Toward this end his education and training must undergo some radical changes. It will have to be directed more to human needs than to technological advances. To be sure, the latter have been dazzling and, in many cases, of incalculable value to mankind, and there will always be need for those who are particularly fitted for such scientific endeavors. But the science of today is not the science of tomorrow, or, as W. Macneile Dixon puts it in "The Human Situation," "Science sheds its last years' conclusions as a snake its skin or a crab its shell." In the last analysis it is the responsibility of the profession to develop individuals who can minister to the spiritual as well as the physical needs of their patients.

In the mad race to achieve recognition in investigational work, the young physician of today is so involved in research projects, which incidentally too often dissipate his time and energies, that he rarely gets to know his patients as he should. He frequently presents evidence of inadequate training in his efforts to assemble an intelligent history and perform an accurate physical examination. This, of course, must be due to defects in the system of teaching as it is presently organized or to insufficiency on the part of the teachers. A discussion of the formal organized instruction of students and hospital resident staffs would be out of place at this time. Just recently this has been well covered by Henry Christian, who pointed out certain undesirable trends in the training of physicians and teachers in internal medicine. I would like, however, to make a few comments on the teachers. In medicine, as in any other field of activity, the ability and attitudes of a teacher are reflected throughout his department; example is a great teacher. Such being the case, a teacher should be eminently qualified by reason of his personal qualities, his professional abilities, and particularly his experience to occupy the position he holds. He should be able to teach a young man to think and to appreciate the importance of learning to write what he thinks with "grace and force." He should set an example in good manners and teach his students to observe the amenities and conventions of a well-disciplined society. The professor's chair in clinical departments is occupied at times by a brilliant young man of parts who has gained recognition as a result of research in some special field. He may or may not possess the attributes required of a clinician, and because of his restricted academic training he lacks the ability to teach bedside medicine on a broad and human level. He has aptly been called a "clinical scientist," and it has been said that his chair is insulated against reality. Medicine may well realize that the man or woman of mature experience has much to offer in the teaching and training of students and that they will fare as well, if not better, in his hands as in those with more basic training perhaps but of tender years. Teachers of clinical medicine should be scientific clinicians rather than "clinical scientists."

Experience in medicine can only be gained through the practice of medicine, and the broader the practice, the better the clinician. Osler has said, "Medicine is learned by the bedside and not in the classroom." If such is the case, then the development of clinicians becomes more and more the responsibility of the profession. One must wonder at times whether we are likely to suffer a dearth of men and women of really great stature in clinical medicine, men who could compare favorably with the Sydenhams, Laennecs, Heberdens, Brights, Addisons, and Oslers of the past. These were men who received their training at the bedside—who realized the proper study of mankind was man and who were developed in the observational school of medicine. In no sense do I mean to disparage the brilliant accomplishments of the true scientist in physiology, pathology, biochemistry, bacteriology, and allied laboratory fields. I would remind the reader that I am speaking of the physician whose duty it is to go about and heal the sick. It is difficult to understand how we could have drifted so far from the natural study of the individual patient to an impersonal, technical analysis of groups of patients when all of the great clinicians of the past were the product of the former school. By their observations and examination of the patient as a human being, rather than as a case, they developed the proficiency that stamped them as great clinicians.

I know there are many who say the physician is better trained today than at any time in the past, that the gen-

V 14
1951

eral practitioner must go because he has fallen by the wayside in the scramble of those who believe they have overtaken and superseded him. But I must ask my challengers—trained in what? Certainly, as I see it, not in the humanities nor in the unchanging values in medicine; not in physical diagnosis, therapeutics, or prognosis. If so, why should the modern young physician require the galaxy of laboratory studies and x-ray examinations, many of them routine and unnecessary? When he secures the results of such tests, how often is he able to properly interpret and correlate them with physical signs and symptoms? I suspect at times the reverse is true—the patient just has to have a certain disease because, according to his reasoning, the x-ray or the laboratory examinations say it must be so. While we all concede that carefully selected laboratory tests and technical procedures can be of assistance in checking a clinical diagnosis, which should be their primary purpose, we must realize that when taken alone they may be very misleading. Only by conferring with the roentgenologist and his colleagues in the laboratory, will the physician avoid serious errors in diagnosis and treatment. It is the well interpreted history and the properly performed physical examination, correlated with the x-ray findings and technical data, that will best determine whether the patient has cancer, colitis, or "nerves," whether his ulcer of the stomach is benign or malignant, or whether his pain in the lower part of the chest means coronary occlusion or biliary colic. And how is one going to evaluate the constitutional, environmental, and psychological factors in a patient's illness without an intimate knowledge of the patient, his secret anxieties, and his family affairs? Such things are not learned to advantage in a class room or even in a hospital. What a rich opportunity the general practitioner has in this respect. Institutional myopia is a difficult malady to overcome, and the physician who is professionally born and raised in an institution will always suffer a handicap as a result of it. There is only one way the young physician can avoid it, and that is by spending several years in general practice. This, I would suggest, should be required of all physicians before they qualify for any specialty—whether it be in a clinical or laboratory field. Specialization by young men, inexperienced in the broad aspects of medicine, carries with it danger to themselves as well as to their patients. As a result of our present system of training, the patient runs the risk of becoming the forgotten man in medicine today. And if there is one unpardonable sin in medicine, it is the failure to consider at all times and with all one's conscience what is best for the patient. I fear there is too much meddlesome medicine and surgery at times that promises more to satisfy scientific interest and curiosity than it does to cure the patient. The employment of medicines or surgical experiments whose effects are not well known and that are fraught with danger to the patient is not in keeping with a conscientious discharge of one's responsibilities. Such practice should be vigorously condemned. Let us vividly remember that "Unless men increase in wisdom as much as in knowledge, increase in knowledge will be an increase in sorrow."

One of the major tragedies of the present generation is the abandonment of the rural life that developed a vigorous sturdy manhood for that of the city, with all its softening, destructive influences. The seed for strong robust manliness must be planted in the country, where the child, who may become the physician, can be exposed to the spiritually uplifting influences of the fields, woods, and streams and where he can grow up with the nobler animals, whose life and manners will exert subtle and strengthening effects on him. Should he make their acquaintance—the spirit of the horse, the tranquillity of the cow, the loyalty of the dog, and even the cockiness of the rooster—all will teach him valuable lessons. Our generation is starving, with all its material riches, for "the bare foot boy with cheeks of tan" who holds a fishing rod in his hand. What a frightening spectacle to behold in his place the frustrated, bespectacled, pale-faced child of the city streets (with his long pants, holster around his waist, and make-believe guns in his hands) whose chief source of play is "cops and robbers" and "cowboys and Indians," whose introduction to literature is the crime and comic strip, whose entertainment is the imbecilic prattle of the radio, the sex and crime of the movies, and, alas, television! Great healers of men do not spring from such environment. Now, of course, all boys cannot be born and raised in the country, but, if humanly possible, they should spend their summers there. And the young physician would do well to broaden his education there, in general practice, where he will have the opportunity of overcoming some of the handicaps of the stereotyped regimented education of which he has been the victim in his earlier years. Such a background will imbue him with respect and reverence for nature and for many of those things that are the mark of a gentleman. I like the sentiment of the autocrat of the breakfast table, who never missed a Sunday at King's Chapel because, as he said, ". . . there is a little plant called Reverence in the corner of my Soul's garden, which I love to have watered about once a week."

I shall now close this paper by giving all the emphasis I can to the final responsibility of the physician to his patient, that is, for him to come out of his smug seclusion and with all the resources and courage at his command to fight for Americanism in medicine. He should realize today, and not tomorrow, that Americanism in medicine is giving way to the false "isms" and demoralizing standards that gain control whenever the true principles of democracy are debauched and destroyed. He should use all his influence to prevent subsidization of his profession by the Federal government. Let him mark the words of Robert A. Millikan, the dean of American scientists, that

> . . . chemistry's story is essentially the same that is told by America's progress during the last 30 years in physics and medicine, in both of which we have risen from far down the line to a top place. It is noteworthy, too, that in that period American science, save for defense projects—the unquestioned responsibility of the Federal government—and for scientific work done by the existing Federal departments, has not been subsidized by the central government, while every country in which science has been so subsidized has lagged far behind us.

With this clearly in mind, let every physician devote his energies toward encouraging the support of our medical schools and hospitals along the lines laid down by Alfred P. Sloan Jr., Chairman of the Board, General Motors Corporation, who emphasizes that private enterprise and corporate support — not centralized government support—should be the solution to our problem.

And it can be, with the magnificent assistance that our profession is receiving from the American Medical Education Foundation, the National Fund for Medical Education, the philanthropic foundations, the life-insurance companies, the pharmaceutical industry, and "big business," as outlined by Mr. Sloane.

The spectacle of what is taking place in this country today should be enough to drop every man to his knees; when all else failed, men of the stature of Washington and Lincoln fell to their knees — are we greater than they? If any one cares to lift an eyebrow at that, let him ponder on the words of Robert A. Millikan, to whom I have referred, who in declaring his belief in God said, "The two supreme elements in human progress are (1) the spirit of religion, (2) the spirit of science (or knowledge)." He goes on to say, "Religion and science . . . are the two great sister forces which have pulled, and are still pulling, mankind onward and upward."

With the collapse of moral standards that is undermining our country, every man should at once assume active and courageous leadership in the righteous fight that lies ahead. Indifference is our peril—let us wake up then, throw it off, and go out in the highways and byways and fight in God's name for our independence, the kind of independence for which our forefathers gave their all. In this way will we best discharge our responsibility to our patients.

Rittenhouse-Plaza.

INFECTIOUS HEPATITIS

LENGTH OF PROTECTION BY IMMUNE SERUM GLOBULIN (GAMMA GLOBULIN) DURING EPIDEMICS

Joseph Stokes Jr., M.D., John A. Farquhar, M.D., Miles E. Drake, M.D., Philadelphia, Richard B. Capps, M.D. Chicago, Charles S. Ward Jr., M.D., Owings Mills, Md.

and

Albert W. Kitts, M.D., Philadelphia

Following the evidence first obtained by Stokes and Neefe [1] that gamma globulin from large pools of plasma, in amounts of 0.15 ml. per pound of body weight, was protective against epidemic hepatitis, there have been numerous confirmatory studies,[2] in some of which a dosage of 0.06 ml. per pound of body weight has been proved to be effective.

Studies were then initiated to determine (1) whether recent batches of gamma globulin were as effective as the batches first used, (2) whether, for the purpose of conserving the material, smaller doses of gamma globulin could be used as effectively, and (3) how long the protection of gamma globulin remained when the persons who had been inoculated continued to be exposed to the disease.

The present report presents the data concerning the above three questions obtained on studies of epidemics of hepatitis within three relatively well-segregated institutions. The problem related to size of effective dose was undertaken in only the last institutional outbreak studied, whereas the problems concerning the effectiveness of more recent batches of globulin and the length of protection during continued exposure were studied in all three institutions.

FIRST INSTITUTION

Description of Institution.—This institution [3] for mentally retarded males was built on the cottage plan with 10 double and two single cottages, giving a total of 22 units. Each unit housed 25 to 50 patients. A diagram of the institution with its water and sewage systems is shown in Chart 1.

The service building, which housed three dining rooms, a large kitchen, and several small store rooms, was located in about the geographical center of the colony. One dining room was used exclusively by the employees, while the other two were used by inmates. Table service in the employees' dining room was provided by mentally high-grade inmates, but the patients' dining rooms had cafeteria service operated by mentally low-grade inmates. Three cottages—No. 1, 6, and 7 (Chart 1)—had their own dining rooms, but inmates from all other units ate in the service building. Food for the entire colony (including the employees' dining room and the three cottage dining rooms) was prepared in the large kitchen in the service building.

The population during the period of study in 1948 consisted of about 849 mentally defective males between the ages of 8 and 75; 779 were white and 70 Negro. The employee population, with an age range of 20 to 75 years, consisted of 157 white men and women (except for one Negro), 113 of whom lived on and 44 off the grounds. They lived in groups of three to 14 on the second floors of the 10 large cottages and the store and administration buildings.

The retarded inmates were employed wherever possible in the operation of the colony in the kitchen and

This work was supported by the commission on liver diseases of the Armed Forces Epidemiological Board, Preventive Medicine Division, Office of the Surgeon General, Washington, D. C.

Read in the Symposium on Liver Disease before the Section on Experimental Medicine and Therapeutics at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

From the Children's Hospital of Philadelphia (Department of Pediatrics, School of Medicine, University of Pennsylvania) (Drs. Stokes, Farquhar, Drake, and Kitts); the Department of Medicine, Northwestern University Medical School and the Liver Research Laboratory, St. Luke's Hospital, Chicago (Dr. Capps); and the Rosewood Training School, Owings Mills, Md. (Dr. Ward).

1. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin: Preliminary Note, J. A. M. A. **127**: 144-145 (Jan. 20) 1945.

2. Gellis, S. S.; Stokes, J., Jr.; Brother, G. M.; Hall, W. M.; Gilmore, H. R.; Beyer, E., and Morrissey, R. A.: The Use of Human Immune Serum Globulin (Gamma Globulin) in Infectious (Epidemic) Hepatitis in the Mediterranean Theater of Operations: Studies on Prophylaxis in 2 Epidemics of Infectious Hepatitis, J. A. M. A. **128**: 1062-1063 (Aug. 11) 1945. Havens, W. P., Jr., and Paul, J. R.: Prevention of Infectious Hepatitis with Gamma Globulin, J. A. M. A. **129**: 270-272 (Sept. 22) 1945.

3. Stokes, J., Jr.: Benjamin K. Ratchford Lectures, University of Cincinnati, Feb. 1 and 2, 1949, unpublished data.

V 147
1951

dining rooms, where they handled food, and on the farm and in the cannery, where they worked with the food and milk supply of the institution.

Two artesian wells supplied the water, but only one (well No. 1 on Chart 1) was in use during the epidemic and for the six months preceding it. Bimonthly water analyses were made, and their results had been satisfactory for several years.

The sewage system of the entire colony drained into a common septic tank. This tank was too small to accommodate the increased institution population, so that the overflow had to be pumped out frequently. Once yearly the entire contents of the tank were pumped out and allowed to drain over the fields used for growing animal fodder, and the tank was cleaned. This procedure was last carried out in May, 1948.

Description of Epidemic.—The first patient with epidemic hepatitis was admitted to the hospital of the institution on May 21, 1948, and all subsequent cases were admitted to the hospital, thus assuring accuracy of recording the incidence. The slow increase in the epidemic, with a peak between Aug. 14 and 30, 1948, is indicated in Chart 2. At the beginning of this peak on Aug. 16 the administration of gamma globulin was started. After Nov. 12 only four jaundiced inmates were admitted—two on Dec. 18, one on Jan. 27, and one on Feb. 1, 1949 Only two of 157 employees acquired hepatitis with jaundice, both cases occurring in July, 1948.

The geographical distribution of the cases showed no consistent pattern, since cases appeared from various parts of the institution at about the same time, except for the detention cottages No. 6 and 7, whose inmates were more isolated, having their own dining rooms. The occupations of the inmates offered no clue as to the origin of the epidemic. Repeated cultures of the water supply failed to reveal any evidence of fecal contamination. The employees and inmates shared a common milk supply, all of which was pasteurized, from the institution's farm.

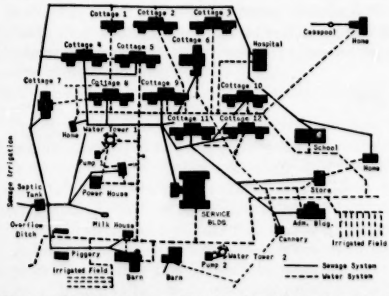


Chart 1.—The first institution. The white dots indicate where the cases of hepatitis occurred.

The clinical picture was entirely consistent with epidemic hepatitis, although the disease in general was mild. The jaundice usually faded rapidly within two weeks of onset. Two deaths had occurred in July, 1948, before we had been requested to investigate the epidemic. Serologic tests for leptospirosis and infectious mononucleosis were carried out with negative findings. The usual liver function tests were conducted with typically positive findings. Stool cultures were negative for pathogenic organisms so far as could be determined.

Gamma Globulin.—For injection of globulin there were eliminated all Negro patients and men over 46 years of age, patients known to have had hepatitis, and the

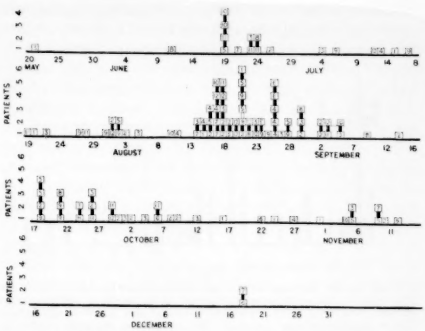


Chart 2.—The first institution. Each square represents one case. The numbers in each square indicate the cottages (Chart 1) from which each case originated.

cottage groups No. 4, 5, 6, and 7 which, at that time, had few or no cases of hepatitis. In the remaining inmates and cottages the groups were divided by selecting alternate inmates alphabetically in each cottage. Gamma globulin, 0.06 ml. per pound of body weight, was injected intramuscularly into 248 inmates, while a slightly larger number, 264, remained as controls, the difference in the size of the two groups resulting from the failure of a small number of persons to appear for their injections. Those in charge of admitting patients with jaundice to the hospital did not know which patients had received the globulin.

It is very probable that many cases of hepatitis without jaundice were not detected and thus not admitted to the hospital, but the ratio of icteric to nonicteric cases would have been expected to be the same in both the control and inoculated groups. However, in the evaluation of gamma globulin, only cases with jaundice were considered.

In the inoculated group of 248, five cases with jaundice (2%) occurred, four in the first five days, and one on the 14th day, after injection. During this same period, four cases of hepatitis without jaundice occurred. No additional cases occurred among the inoculated group, although, among the 264 controls, cases with jaundice continued to occur for seven months; 44 cases in all (17%) as indicated in Charts 2 and 3. Since gamma globulin usually does not begin to protect until about five days after its injection, the difference becomes even more striking if the four early cases are omitted. If the same five-day period is omitted from the controls, the ratio of comparison of cases then becomes 0.4% in the inoculated group to 15% in the controls. The average duration of jaundice in the inoculated group was 14.2 days, while in the control group it was 16.2 days. Only 30% of the jaundice cases occurred in patients under 20

years of age; while 30% of the total inmates were in this same age group.

There was no evidence to suggest any lengthening of the incubation period as a result of the globulin administration.

Test of Resistance.—With the approval of their guardians and parents, and in view of the mild nature of this epidemic, 50 of the inoculated group together with

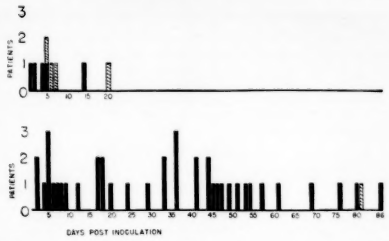


Chart 3.—The first institution. This Chart represents approximately the first three months of the hepatitis epidemic in the inoculated and the control groups. The solid blocks represent hepatitis with jaundice; the striped blocks, hepatitis without jaundice. The top portion represents the inoculated group; the bottom portion, the control group.

4 volunteer prisoners at another institution as controls were tested for immunity to the homologous virus nine months after the epidemic by giving infective serum from the same epidemic orally to both groups. In six of the inmates (12%) mild hepatitis with jaundice developed after the usual incubation period, while in one of the volunteers hepatitis with jaundice and in three hepatitis without jaundice developed.

For various reasons it was not possible to test the resistance of a random sample of the 264 control inmates.

SECOND INSTITUTION

The epidemic in the second institution, studied chiefly during 1949, is being reported elsewhere [4] in more detail because its study involved many more than the three problems with which this report is concerned.

Description of Institution.—This is a large city orphanage where orphan infants are admitted, and where mothers are delivered. Children do not remain after 3 years of age. Graduate nurses, in small number, train student nurses for the career of "practical nursing."

Description of Epidemic and Use of Gamma Globulin.—Hepatitis with jaundice which was not due to leptospirosis or infectious mononucleosis had occurred in increasing incidence among new student nurses since 1942. Late in 1948 one of us was apprised of the situation which obviously suggested an endemic focus of infection. At this time, Nov. 7, 1948, the inoculation with gamma globulin (.06 ml. per pound body weight) of all incoming student nurses was advised and carried out according to Table 1. All of these nurses were inoculated within one to one and one-half months after the start of their training at the orphanage. On Aug. 29, 1949, the globulin inoculation of incoming student nurses was stopped.

The following paragraph indicates the history of hepatitis in the institution before the use of globulin, during the use of globulin, and in the nurses admitted to training after Aug. 29, 1949, when the use of globulin was stopped. During the period Jan. 1, 1946, to Nov. 7, 1948, forty-four of 139 (32%) new student nurses acquired hepatitis with jaundice. During the use of globulin, when 36 students were admitted in training, one case of jaundice occurred, in a student nurse who had received her injection only two days preceding the onset of hepatitis, thus indicating the virus was still active during this period. Among 20 new students admitted in training after Aug. 29, 1949, there were six cases of hepatitis with jaundice and three cases of hepatitis without jaundice (45%) before Jan. 1, 1950. Among the 35 student nurses who had previously received gamma globulin and had remained on duty under similar conditions to those obtaining for the nurses admitted after Aug. 29, 1949, one contracted hepatitis with jaundice. This nurse was admitted on March 14, 1949, was inoculated with globulin on April 23, and jaundice developed on Dec. 20. By chance she did not serve until Oct. 15, 1949, on the fourth floor, where the endemic disease appeared to be most prevalent among the infants, and in relation to which floor the hepatitis among the nurses was most apt to occur.[5]

With certain changes in nursing techniques carried out in December, 1949, and reported elsewhere,[5] no cases of hepatitis with jaundice have since occurred among the nurses.

THIRD INSTITUTION

Description of Institution.—The third institution studied in 1950 is a relatively well-segregated State Training School for girls and boys, to which access was obtained at an early stage of a hepatitis epidemic in two cottages, one for girls and one for boys. Leptospirosis and infectious mononucleosis had been eliminated as etiological factors by the usual serologic tests. The cottages provided all their own food, playrooms, and lodging, and thus offered an excellent opportunity for a controlled study. The girls' cottage housed 87, the boys' 85, all ranging in age from 4 to 14 years.

TABLE 1.—*Number of Nurses and Dates of Injections with Gamma Globulin*

Dates of Injections	Number of Nurses
Nov. 4, 1948	6
Jan. 31, 1949	10
April 15, 1949	3
April 23, 1949	6
May 11, 1949	6
June 21, 1949	4
June 28, 1949	1
Total	36

Description of Epidemic and Use of Gamma Globulin.—The dose of gamma globulin was reduced to one-sixth of that usually given, namely, to 0.01 ml. per pound of body weight. Those to be inoculated were selected alphabetically. That a random selection was attained is indicated by the similar ages, the similar dates of admission

4. Capps, R. B.; Bennett, A. M., and Stokes, J., Jr.: Endemic Infectious Hepatitis in an Infants' Orphanage: Epidemiologic Studies in Student Nurses, to be published.

5. Bennett, A. M.; Capps, R. B.; Drake, M. E.; Ettinger, R. H.; Mills, E. H., and Stokes, J., Jr.: Endemic Infectious Hepatitis in an Infants' Orphanage: Epidemiologic Studies in Infants and Small Children, to be published.

V 14
1951

to the cottages, and the similar distribution of beds in the sleeping quarters of the groups. All the boys, and all the girls, respectively, remained in intimate contact over the period of 10 months of the study except when isolated as a result of hepatitis. Also 54 adult employees and attendants were given the same dosage of globulin at the request of the administration, while six employees refused it. These adults lived in separate quarters provided for them on the institution's grounds, and many ate one or more meals a day in the cafeteria of the institution to which the children did not have access.

TABLE 2.—*Incidence of Hepatitis with Jaundice, Month by Month, in the Inoculated and Control Groups* at the Rosewood State Training School, 1950*

	Total No. in Group	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.
Boys										
Control	29	3	5	2	2	1	2	2	5	0
G. G.†	34	1**	1‡	0	0	0	0	0	0	0
Girls										
Control	48	0	4	0	2	0	0	8	3	3
G. G.†	18	0	0	0	0	0	0	0	0	0
Employees										
Control	6	0	0	0	0	1	0	2	0	0
G. G.†	54	0	0	0	0	0	0	1	0	0

* Injections carried out on June 12, 1950.
† G. G. = gamma globulin.
** 9 days after gamma globulin.
‡ 18 days after gamma globulin.

It is seen from Table 2 that there were 22 cases of hepatitis with jaundice in the 29 boys who served as controls, and two cases among the group of 34 receiving gamma globulin. In one of these hepatitis developed with jaundice 9 days and in the other 18 days after receiving the globulin. Among the 48 girls who served as controls, there were 20 cases of hepatitis with jaundice, and there were none in the 18 who received gamma globulin. Among the 54 employees who received gamma globulin, one case of hepatitis with jaundice occurred seven months later, while in the six who received no gamma globulin there were three cases of hepatitis with jaundice.

A summation of these data indicates that there were 45 cases of hepatitis with jaundice in the 83 controls, and three cases among the 106 children and adults receiving gamma globulin.

COMMENT

The question raised as to whether more recent batches of gamma globulin are as highly protective as the older ones used in previous studies has a clear-cut affirmative answer from the data here presented of the three epidemics studied. Also, the excellent protection afforded by the small dose (0.01 ml. per pound of body weight) of globulin used in the last institution studied, strongly suggests that gamma globulin may be conserved to the extent indicated in this study whenever protection is desired against epidemic hepatitis. Confirmation of the value of this small dosage for protection is still required.

In the three institutions the mode of transmission appeared to be the fecal oral route, since the lack of an explosive outbreak did not suggest milk, food, or water contamination.

The outstanding finding was the length of protection afforded by the gamma globulin despite the continuation of the epidemic disease among the control groups in the three relatively closed institutions. In the first institution no case with jaundice occurred in the inoculated group after the 14th day following injection, while among the control group cases continued to occur actively for five months and sporadically for two additional months. In the second institution, only one case with jaundice (3%) occurred after the second day following injection, despite an exposure three to four times longer than that of the controls; whereas six cases with jaundice and three cases without jaundice (45%) occurred among the control group of 20 new uninoculated student nurses, exposed for approximately three months under the same conditions as those obtaining for the inoculated group. In the third institution, among the boys and girls in the two cottages studied no recognized case of hepatitis occurred after the 18th day following inoculation, over the succeeding eight months of continuous exposure to cases of jaundice among the controls, who had 39 cases of jaundice well distributed over the same eight-month period.

Such prolonged protection in inmates of the three institutions from a single dose of gamma globulin, despite continued intimate exposure, could be explained in one of three ways:

1. Active Immunity: It is conceivable that the gamma globulin used contained a mixture of epidemic hepatitis virus and its neutralizing antibody and that a neutralized antigen-antibody mixture was dissociated by dilution following injection with the release of sufficient active antigen to produce active immunity, but not sufficient to produce frank disease.

This possibility may be considered as unlikely for the following reasons:

1. The later test of resistance of 50 of those boys who received gamma globulin in the first institution indicated that at least six were susceptible to frank disease. If the gamma globulin were an actively immunizing agent, such boys also should have been protected. However, it is conceivable that such an immunizing agent would not have protected all of the boys inoculated.

2. Neutralized mixtures of virus antigen and antibody in other viral diseases have not served well as immunizing agents, particularly when the virus is "covered" by a large excess of neutralizing antibody.

3. If it were a neutralized mixture from which virus was released after injection, gamma globulin on occasion should produce frank hepatitis. This has not been recorded in the gamma globulin used in the United States.

2. Passive Immunity: It is conceivable that the amount of antibody present in the single dose used was sufficient to protect the inoculated groups against hepatitis which continued to occur in the controls and in the rest of the institutions over five, nine, and eight-month periods of intimate exposure to the other cases in their common dormitories, dining rooms, workrooms, playrooms, and hospital wards. That the persistence of homologous protective antibody depends primarily on its initial titer appears very probable when one compares the short length of protection (four to five weeks) against measles afforded by the usual small protective dose of gamma globulin, with the five to seven month protection afforded by the far larger transfer of measles antibodies from an immune mother through the placenta. For protection against epidemic hepatitis, it is possible that the usual

dose of gamma globulin might be relatively equivalent to the height of the transplacental antibodies of measles, and therefore remain effective for several months. In other words, a remaining trace of injected gamma globulin after several months might still be protective against hepatitis, although not protective against measles. Serologic tests are not available for such determinations, and the present epidemiologic data bearing on this point are insufficient. In the study conducted in the first institution it is difficult to believe that traces of injected globulin would remain after nine months. (In order to test this possibility, a study has been projected in which a large group of volunteers inoculated at the same time with gamma globulin, 0.06 ml. per pound of body weight, would be divided into several small groups. The resistance of these small groups would then be tested by inoculating them, one group at a time, at successive two to three month intervals with natural virus orally; namely, at about 3, 6, 9, 12, and 15 months, respectively, following the time of injection of the globulin. The limitation of available volunteers has thus far prevented this study.)

However, were passive immunity alone the reason for the absence of hepatitis in the inoculated group, then more than six cases of the disease would have been expected in the group of 50 previously inoculated boys whose resistance was tested following the epidemic in the first institution. Among the four volunteers from another institution who acted as controls for this test of resistance, in one hepatitis with jaundice developed and the remaining three had clinical hepatitis without jaundice; i. e., apparently 100% "takes." In all recorded experience with young volunteers, or, for example, in epidemics where severe exposure to a water-borne virus has occurred, which represents a situation quite similar to the present test of resistance, in at least 45 to 50% of the exposed group hepatitis with jaundice has developed.

In this epidemic there was no higher incidence of jaundice in the younger groups than in the older groups, thus indicating that the institution apparently was virgin soil for the hepatitis virus.

Among inmates who had been present during the epidemic, jaundice continued to occur sporadically for over one and one-half years following the epidemic, thus indicating that maximal exposure had not occurred during the epidemic.

In the epidemic recorded by Neefe and Stokes [6] the percentage of jaundice recorded (255 of 572) was 46, whereas in the third epidemic recorded in the present report the control groups had an over-all incidence of hepatitis with jaundice of 51%. Also, in a school epidemic mentioned by Brown [7] the percentage of jaundice recorded (41 of 74) was 55. Such epidemics probably represent almost maximal exposure, and in the present test of resistance of the 50 boys, obviously there was direct exposure of all the boys to considerable amounts of virus. Thus, since jaundice has been used here as a final criterion for disease and since about 50% of young volunteers, as shown in previous studies, will usually acquire jaundice after oral infection with the infectious hepatitis virus, the anticipated number of jaundiced cases in this group of 50 boys would have been approximately 20 to 25, unless some mechanism producing immunity was operative.

3. Active Immunity Superimposed on Passive Immunity: A final explanation, and, apparently, the most plausible, is that the continuous exposure of the inoculated groups, in their common dormitories, dining rooms, playrooms, and wards, to the virus in the cases occurring among the control groups produced an active immunity superimposed on a waning passive immunity in the inoculated group without the occurrence of any apparent disease among them.

Were it not for this possible method for development of active immunity, it would be difficult to explain the absence of hepatitis with jaundice in 44 of 50 inoculated boys in the first institution whose resistance was tested later by means of ingestion of the homologous virus.

In the second and third institutions the evidence for such production of passive-active immunization is even more strongly suggestive, inasmuch as the inoculated groups were completely protected (after nine days from the time of injection with two exceptions) for approximately nine and eight months, respectively, during continued exposure to virus under natural conditions. In the first of these two institutions, the exposure of the inoculated nurses was as similar to the exposure of the controls as it was possible to attain under the usual nursing assignments, except that the inoculated group was exposed for a longer period. In the other institution the exposure of the groups studied may be considered as practically identical, since the dormitories, dining rooms, and playrooms were all used in common by the children of both the inoculated and the control groups.

If this final explanation is the correct one, which we believe it is, then this method of apparently producing a passive-active immunization under natural conditions in the field with respect to a viral infection offers the possibility of similar studies of other viral diseases which may produce permanent immunity.

Hitherto, gamma globulin or homologous antibodies have not been used in man, to our knowledge, for such immunization. However, use has been made in man of transplacental passive transfer of antibody for the study of such immunization in measles by Herrman.[8] Over the period from 1914 to 1922 he obtained suggestive evidence that transplacental antibodies might be utilized at a suitable point in their decline to permit mild symptoms of measles on exposure to the natural virus and yet at the same time to produce a resultant permanent immunity. In Herrman's studies a potentially dangerous method was used, exposing infants during the first six months of life to nasal secretions obtained from acute cases of measles 24 hours before the eruption appeared. In 165 infants thus directly exposed, preferably in the fourth to fifth month of life, mild increases of temperature occurred between the eighth to 16th day after exposure, with or without a slight maculo-papular eruption on the

6. Neefe, J. R., and Stokes, J., Jr.: An Epidemic of Infectious Hepatitis Apparently Due to a Water Borne Agent: Epidemiologic Observations and Transmission Experiments in Human Volunteers, J. A. M. A. **128**: 1063-1075 (Aug. 11) 1945.

7. Brown, G. C.: The Possible Significance of Milk and Water in the Spread of Virus Infections, Am. J. Pub. Health **39**: 764-771, 1949.

8. Herrman, C.: Immunization Against Measles, Arch. Pediat. **39**: 607-610 (Aug.) 1922.

V 147
1951

face in 84 infants. Of 75 of these 165 infants who were followed for four to eight years, five had measles on exposure, while the remaining 70 failed to have measles, despite family exposure in 45 instances. Also, 36 of these children were reinoculated later with the natural virus, obtained as previously described from active cases, and measles occurred in none of them. In view of the high incidence of natural measles, such results appear encouraging, although much larger numbers would have to be studied in order to obtain conclusive evidence. The major difficulties with Herrman's method are (1) the lack of a serologic test to insure immunity in the mother and thus a possible exposure of the infant to measles at an age period when the disease may be more severe, and (2) the possible presence of other pathogens, such as poliomyelitis virus, in the nasal secretions of the patients with acute cases of measles used as donors of virus.

The advantage of the method described in the present report is the opportunity offered by such a material as gamma globulin for possible selection both of a suitable amount of antibody and of a suitable time to inject the globulin, when an epidemic is present, or when immunization appears to be most suitable for the infant or child. The natural virus can then enter, or may be inoculated, by its natural route.

The use of viral infections of animals for passive-active immunization appears to strengthen the above strongly suggestive data concerning man, at least so far as the possibility is concerned of producing an active immunity superimposed on a waning transplacental passive immunity. Enders and Hammon [9] in 1939, reporting on panleukopenia of cats, suggested that passive-active immunization was a possibility in this viral disease (although without confirmatory data) as follows:

> This immunity of the kitten appears to be most easily accounted for *a priori* by a passive transfer of protective substance across the placenta. The duration of this type of immunity under effective isolation would at best be only a few months, but it would seem likely that when frequent exposure to the virus occurs, active immunity might fortify a waning passive immunity. A chain of events of this sort could account for the fact, which we have noted, that relatively few manifest cases of this disease are seen in a community where it is endemic.

On the other hand, two viral infections of animals in which passive-active immunization by means of utilizing the natural transplacental-passive immunity has been conclusively demonstrated are mouse encephalomyelitis virus (MM strain) infection and ectromelia of mice. In the case of the MM virus Curley and Gordon in particular [10] and later Anderson and Bolin [11] have shown that litters born to immune mothers could in turn be actively immunized by inoculations of natural virus at the proper times and in suitable amounts. It was shown also by the former workers that the females of such immunized litters on reaching adulthood would in turn passively immunize their progeny of the second generation.

Fenner's [12] recent study of ectromelia has been particularly enlightening in that he demonstrated such a passive-active immunization by complete survival, following test of resistance, of all litters born to immune mothers and then exposed to natural virus, and complete loss of all litters born to susceptible mothers. In the passively immunized litters exposed to natural virus, with the superimposing of an active immunity, inapparent disease developed, as demonstrated by the detection of a few viral bodies in the blood, spleen, and liver without symptoms at the end of the usual incubation period.

If the method of passive-active immunization in certain viral diseases either in human newborns or in older children by means of gamma globulin becomes practicable, the limitations for such methods in each disease must be quite different and would require careful analysis. In such an analysis the importance of the passive transfer of antibodies through breast milk or through heterologous milk would require investigation. It would appear that those viral diseases which produce permanent immunity would best lend themselves to such study, although, even in such viral diseases as epidemic influenza, when the level of antibodies is sufficiently elevated, repeated stimulation of active immunity with virus inoculated by the natural route deserves investigation. Some studies [13] in respect to mumps have already been conducted in this clinic during the newborn period, with early findings which are not incompatible with the evidence here presented for passive-active immunization.

SUMMARY AND CONCLUSIONS

Gamma globulin of recent batches has been shown to be highly protective in passive immunization against viral hepatitis in three institutional epidemics. In the third institution there was clear-cut evidence that as small a dosage of globulin as 0.01 ml. per pound of body weight was protective.

The single injection of globulin used in the three institutions caused protection of the inoculated groups for at least five, nine, and eight months, respectively, despite their continued intimate exposure to continuing cases of hepatitis in the control groups. It is conceivable, but not probable, that traces of gamma globulin remaining in the circulation or attached to tissue cells for such five, nine, and eight-month periods might be responsible for such protection.

The greater probability exists, however, that the waning passive immunity afforded the opportunity for inapparent or subclinical infections among the inoculated groups which resulted in active immunity superimposed on the passive immunity, or, in other words, a resultant passive-active immunization. Results of animal viral studies in litters born to immune mothers and exposed to natural virus are compatible with such an explanation.

The possible uses of passive-active immunization in viral diseases in both the newborn period and during childhood, in either the presence or the absence of epidemics, by means of immune bodies are discussed.

1740 Bainbridge St. (Dr. Stokes).

9. Enders, J. F., and Hammon, W. D.: Active and Passive Immunization Against Virus of Malignant Panleucopenia of Cats, Proc. Soc. Exper. Biol. & Med. **43**: 194-200, 1940.

10. Curley, F. J., and Gordon, J. E.: Immunization of Young Mice with Unmodified M M Mouse Encephalomyelitis Virus Under Passive Protection from Immune Mothers, Am. J. Hyg. **48**: 81-86, 1948.

11. Anderson, J. A., and Bolin, V.: Congenital Antiviral Immunity in Swiss Mice, Am. J. Hyg. **50**: 200-206, 1949.

12. Fenner, F.: Mouse-Pox (Infectious Ectromelia of Mice): Review, J. Immunol. **63**: 341-373, 1949.

13. Stokes, J., Jr.: Frederick Packard Memorial Lecture, Philadelphia, Nov. 14, 1950, unpublished data.

CHANGING ATTITUDE TOWARD MULTIPLE SCLEROSIS

A PROGRAM OF MANAGEMENT

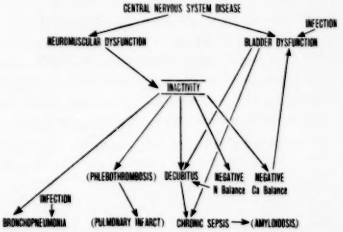
Edward E. Gordon, M.D.
and
Karl E. Carlson, M.D., New York

The attitude toward the course of multiple sclerosis is undergoing a change.[1] "The classic" picture has emphasized the rapid progression, the swift onset of helplessness and early death. While such a portrait may apply to an individual case, it appears that the natural evolution, like the symptoms of the disease, is varied, and that many patients do retain usefulness for a long period of time. Moreover, when multiple sclerosis is studied in a group, the survival time appears to have been underrated; one recent statistical study indicates that the median duration of the disease is in the vicinity of 27 years,[2] a surprisingly high estimate in comparison with previous views.

No prediction as to immediate course and prognosis is possible in each individual case. Every patient must be given the benefit of the doubt to as liberal an extent as the judgment of the physician can permit. No one can foretell whether a given remission may not be the last, or whether it will not be maintained for many years. Therefore, it is necessary for the physician to proceed as if a remission were the final one. He must foster a spirit of hopeful management and exploit every device to improve the patient's situation. To this end, the techniques developed in the field of rehabilitation may be utilized to teach the patient how to live with his residual capacities to the best of his ability.

It is generally conceded that physical medicine often is the most useful approach to the management of patients with chronic neurological diseases.[3] This statement should be broadened to include suitable rehabilitative techniques. The application of this branch of medicine is all the more important because of failure of any definitive medical treatment up to the present time. But treatment by default represents only a negative approach. Already mentioned is the necessity for regarding each individual patient as a possible candidate for rehabilitation, since one cannot determine the future course of the disease as regards speed of progression. There is yet another justification for the management of multiple sclerosis by rehabilitative techniques, and that is the advantage of maintaining maximum physical activity.

The chief cause of death in multiple sclerosis is broncho-pneumonia.[4] One wonders, in view of the ultimate immobilization, whether thrombophlebitis and consequent pulmonary infarction do not also occur. Among important contributory causes are decubitus ulcers, leading to chronic sepsis, and urinary tract infection. The latter condition, though primarily due to loss of bladder motility, may be aggravated by osteoporosis and renal calcinosis, known to occur in traumatic paraplegia.[5] Of extreme importance is the recent observation of the occurrence of amyloidosis in paraplegics with extensive decubitus ulcers and urinary sepsis.[6] Inactivity appears to be an important underlying factor in the development of bronchopneumonia, decubitus ulcers and kidney stones (Chart). Does enforced immobilization, therefore, materially contribute to and hasten death? Is it possible that the course of the disease may be influenced to the extent of prolongation of life by the encouragement and promotion of activity for as long as possible? These questions cannot be answered at present; they challenge the physician who is seeking a rational approach to the management of multiple sclerosis.



Schematic representation of various causes of death in this disease. Conditions in parentheses are hypothetical for multiple sclerosis.

In the management of this disease by rehabilitative techniques the broad strategy is directed toward teaching the patient how to manage his life in spite of his handicaps and by means of his residual abilities. The problem is one of calling into play reserve functions and of developing substitution devices. Obviously, the primary pathological process cannot be influenced by peripheral manipulations. It is hoped that by utilization of residual functions the patient's life may be made productive; if not productive, self-dependent; if not self-dependent, at least tolerable.

The techniques employed to realize these aims can be summarized briefly as follows: (1) strengthening of residual motor units of a muscle which are only partially

A monograph in elaboration of this paper can be obtained on request from the National Multiple Sclerosis Society, 270 Park Ave., New York 1.

Read before the Section on Physical Medicine and Rehabilitation at the One Hundredth Annual Session of the American Medical Association, Atlantic City, New Jersey, June 13, 1951.

1. Gordon, E. E.: Multiple Sclerosis: Application of Rehabilitation Techniques, New York, National Multiple Sclerosis Society, 1951.
2. Limburg, C. C.: The Geographic Distribution of Multiple Sclerosis and Its Estimated Prevalence in the United States, A. Res. Nerv. & Ment. Dis., Proc. **28**: 15, 1950.
3. Schlesinger, E. B.: Pharmacological Agents in the Treatment of Neuromuscular Disorders, Phys. Therapy Rev. **28**: 100, 1948. Fay, T.: The Neurophysical Aspects of Therapy in Cerebral Palsy, Arch. Phys. Med. **29**: 327 (June) 1948.
4. Schumacher, G. A.: Multiple Sclerosis, J. A. M. A. **143**: 1059 (July 22) 1950.
5. Abramson, A. S.: Bone Disturbances in Injuries to the Spinal Cord and Cauda Equina (Paraplegia): Their Prevention by Ambulation, J. Bone & Joint Surg. **30-A**: 982, 1948.
6. Unpublished data.

removed from voluntary innervation but which are atrophied from disuse; (2) training of synergists for a particular motor pattern in which the neuronal connections to the prime mover are affected; (3) training of other muscles to perform movements to substitute for the normal prime movers irreversibly affected; (4) use of mechanical devices to compensate for disabilities in order to accomplish purposeful motion required for the numerous activities of daily living.

The method here described is commonly called "muscle re-education." However, it is evident that one cannot separate the training of muscles from that of the whole central nervous system. This training process entails the establishment of motor patterns centrally, the muscles being merely effectors of a functional system. It may, therefore, be referred to more properly as "neuromuscular re-education."

In order to establish a program for neuromuscular re-education, a detailed inventory of the disabilities must be made. It would be more nearly exact to say that the extent of the capabilities must be known, as a training program is designed to exploit residual function. This inventory relies upon two orders of information: the specific neuromuscular findings, and the over-all motor functions involved in executing the ordinary business of everyday living.

The data relating to the specific neuromuscular status are derived from detailed testing of muscle groups and the joints which they activate. This includes tests for motor ability, spasticity, and joint range of motion. In this way one may assess the presence and degree of spasticity, muscle strength and contractures. It is beyond the scope of this paper to present the exact methods of these examinations; they represent the common tools of the worker in rehabilitation. Testing for incoordination is also essential, since its presence will influence the decision against starting training for ambulation with crutches. Another important neuromuscular deficiency to be kept in mind is that occurring in bladder disturbances. Such a deficiency usually occurs somewhat late in the course of the disease.

The second order of information relates to tests for functional capacity, in which a series of purposeful, integrated movements is carried out by the patient. This type of testing includes a battery of activities covering body positioning, reach and grasp, and progression, such as one would ordinarily do at home, at work, in travel and at play. It includes a wide assortment of items to approximate a complete picture of the patient's motor capacities. This test for activities of daily living may be regarded as a test of functional performance.[7] The results derived from these tests will form the basis of the training program to increase the scope of the patient's capabilities.

In addition to the physical evaluation, the mental state, the attitude and temperament of the patient should also be known. Social adjustment is equally as important as physical potential. Without the cooperation of the patient the arduous training which rehabilitation demands will fail. At this point it may be pointed out that the occurrence of outbursts of laughing and crying does not militate against a program of training. They are largely motor manifestations which do not represent "emotional instability," since no corresponding change in mood content is associated with these outbursts. A better term would be "emotional lability." During the course of the management of an individual, a discussion of the patient's disease will inevitably arise. For most patients it is recommended that the problem be met realistically and honestly. Multiple sclerosis need not have terrifying implications if the optimistic side be stressed, such as the relatively long life expectancy and the possibility of spontaneous arrest of the process.

A program of retraining must set realistic objectives on the basis of the severity of impairment. A suggested working evaluation of the patient should be based on whether he is (1) independently ambulatory; (2) ambulatory with aids (cane, brace, crutches); (3) restricted to a wheel chair, or (4) confined to bed.

With this classification in mind, one seeks either to improve or maintain function within a particular category, or to raise the functioning level to the next higher grade. To achieve this, deficiencies in integrated movement (e. g., inability to bring hand to mouth) are correlated with specific neuromuscular disabilities of the upper extremity—disturbances of grasp, supination, elbow flexion, and abduction of the shoulder due to certain combinations of weakness, spasticity and contractures, both of the muscles responsible for these motions and of their antagonists. Deficiencies in integrated motion have been assessed by ADL tests; while impairment of individual muscle groups and the relevant joints has been evaluated by the specific neuromuscular tests. The data thus derived will point the way to an individualized program, which in general is designed to improve strength and minimize spasticity and contracture, thus allowing the synthesis of individual movements into integrated purposeful motions of a whole limb or limbs. If incoordination complicates the picture, training directed toward this symptom is also included. If, in spite of the above measures, no practical improvement is forthcoming, mechanical aids may be utilized wherever possible to bring various activities of daily living within the possibility of performance. Residual capacities are the driving force for these self-help devices.

The specific details of a training program are too lengthy to be presented in this report. Measures against spasticity, muscle weakness, contractures and incoordination are part of the armamentarium of physical medicine. Night splints to prevent or correct drop foot, wristdrop or knee flexion may be mentioned here for emphasis. An excellent paper on training for the activities of daily living has already been published.[8] It is appropriate to mention the techniques elaborated by Kabat in treatment of neuromuscular dysfunction including multiple sclerosis.[9] These techniques evoke repeated maximal effort of the paretic limbs against heavy weights for two

7. Deaver, G. G., and Brown, M. E.: Physical Demands of Daily Life: An Objective Scale for Rating the Orthopedically Exceptional, New York, Institute for the Crippled and Disabled, 1945.

8. Buchwald, E.: Functional Training, Phys. Therapy Rev. **29**: 491, 1949.

9. Kabat, H.: Studies on Neuromuscular Dysfunction: New Principles of Neuromuscular Reeducation, Permanente Found. M. Bull. **5**: 111, 1947; Studies on Neuromuscular Dysfunction: Rhythmic Stabilization; A New and More Effective Technique for Treatment of Paralysis Through a Cerebellar Mechanism, ibid. **8**: 9, 1950. Cailliet, R.: The Rehabilitation Treatment of Multiple Sclerosis and Its Rationale, Occup. Therap. **29**: 1, 1950.

to three hours daily. It would appear from this author's observations that improvement in motor performance could be attributed not only to increased strength of muscles atrophied by disuse but also to improvement in volitional control as well as to reduction of the associated spasticity. Gains appear to be held, moreover, provided the patient continues with the active program. More data from other clinics are necessary.

In addition to procedures of physiotherapy, many patients may gain by the pursuit of hobbies. These pursuits afford another method for carrying out integrated motions with the added advantage of combining purpose with interest. Various arts and crafts instruction manuals for beginners are available at modest cost.

If upper extremities are equal to the task and incoordination is no problem, a trial of crutch walking should be considered when ambulation otherwise is not safe. It is true that diffuse involvement is the rule in multiple sclerosis and will militate against this form of walking, but a dogmatic view may lead to deprivation of a patient's right to every resort to extend his range of performance. Teaching crutch gaits requires a knowledge of the underlying general principles and is a tedious task.[10] Along with crutches, braces will usually be necessary to maintain normal postural relationships otherwise impossible due to unstable ankle joints, knee joints, or both. The physician should have a working knowledge of braces and not leave the prescription entirely in the hands of the brace maker. In multiple sclerosis, owing to strong spasticity of the gastrocnemius, an efficient type of brace includes a stirrup type of attachment to the shoe, rather than a caliper attachment. The former affords more stability and its axis of rotation is at a physiological position in line with the ankle joint. The brace embodies two lateral bars of duralumin® or surgical steel and is equipped with an ankle stop to prevent plantar flexion beyond 90 to 95 degrees. Braces employing steel spring wires to act as a stop are inadequate to hold against the force of a spastic gastrocnemius.

If ambulation with aids proves not feasible, progression in a wheel chair should be considered. Choice of this equipment is not by taste, as in the case of a car, but by the necessities of the situation. There are 22 considerations that may be taken into account in prescribing a wheel chair and accessories, and these are determined by the residual functions. For example, the power of propulsion is ordinarily provided largely by the elbow extensors with the hands placed anterior to the axis of the wheel. If extension is weak but flexion adequate, the back of the wheel chair should adjust to an angle of 33 degrees with the vertical. This position facilitates placing the hands on the rear of the wheel and developing the force for propulsion by biceps flexion. Manufacturers provide many other accessories by means of which the abilities of the patient can be exploited. Since the patient is to spend the major part of his life in a wheel chair, fairly accurate measurements for the proper dimensions of the basic chair frame are essential.

Besides the well-known mechanical devices such as crutches, braces, wheel chairs, there are available many supplementary tools to enhance reach and grasp capacities. The list of such mechanical aids is limited only by imagination and ingenuity. A whole science of self-help devices has been developed in the interests of patients with residual but deficient motor abilities. Large grasping surfaces overcome the problem of weak grasp; a splint affixed to the hand and accommodating various implements substitutes for lack of grasp. Booklets describing in detail the design and cost of a large number of such devices are available.[11]

Bladder disturbances are frequent enough to warrant attention. In attempting rehabilitation, efforts must be directed toward controlling incontinence, for it may represent to the patient as serious a problem as the accompanying paralysis of his legs and may cause him to withdraw from all social contact. Efforts are directed toward establishing a reflex bladder, which is the optimal result when the suprasegmental innervation is destroyed. To attain a reflex bladder, automatic tidal drainage or intermittent manual irrigations must be instituted. These procedures prevent overdistension or shrinkage and promote effective emptying contractions in the presence of 200 to 400 ml. of fluid. When urological investigation establishes freedom from urinary infection as well as the presence of good bladder capacity and forceful contractions, bladder training is attempted. Briefly, this procedure allows spontaneous emptying on a reflex basis with progressively increasing periods of nonvoiding until three-hour intervals have been attained. The technique and results of bladder retraining in traumatic paraplegia have already been well described [12]; a similar approach should be attempted in selected patients with multiple sclerosis.

Other common urinary symptoms besides incontinence are urgency and difficulty in starting the stream. Since these symptoms may denote the onset of impaired bladder motility, it is suggested that some consideration be given to early urological investigation of "mild" complaints with the hope of delaying or preventing the sequelae of urinary infection and atonic bladder.

Finally, the physician should promote good hygiene, both mental and physical. Resolution of anxieties may lead to decrease in spasticity. Some patients may need corrective psychotherapy, for it has been found that many multiple sclerotics have basic neurotic traits which warrant attention. Sound principles of proper living, eating, and sleeping apply in this disease as in any other chronic condition.

The following two case reports are presented to illustrate the application and objectives of a rehabilitation program. No attempt is made to evaluate the benefits of such a program at present; it is presented only as a challenge to the physician to consider a patient with multiple sclerosis beyond the mere requirements of diagnosis, which, after all, are only preliminary steps. It is conceded that the possibility of remissions serves to vitiate any well-founded conclusions. However, the in-

10. Deaver, G. G., and Brown, M.: The Challenge of Crutches, New York, Institute for the Crippled and Disabled, 1950.

11. Self-Help Devices for Rehabilitation, Institute of Physical Medicine and Rehabilitation, New York, New York University-Bellevue Medical Center.

12. Munro, D.: The Rehabilitation of Patients Totally Paralyzed below the Waist, with Special Reference to Making Them Ambulatory and Capable of Earning Their Living: Control of Urination, New England J. Med. **234**: 207, 1946; The Rehabilitation of Patients Totally Paralyzed below the Waist, with Special Reference to Making Them Ambulatory and Capable of Earning Their Living: Tidal Drainage, Cystometry and Bladder Training, ibid. **236**: 223, 1947.

V 147
1951

crease in performance, demonstrated in these case reports was independent of any change in the symptoms of the disease, but was based upon exploitation of available capacities which otherwise would have lain fallow.

REPORT OF CASES

CASE 1.—J. M., a 30-year-old white housewife, was diagnosed as having multiple sclerosis in 1944, at which time she developed numbness of her right hand and weakness of her lower extremities. The weakness of her legs progressed to the point at which she became confined almost entirely to her wheel chair. Three years before she had developed pulmonary tuberculosis which was treated by absolute bed rest for a period of six months. During this period, she developed severe flexion contractures of her hips, knees, and ankles which made her ability to get from bed to wheel chair a physical impossibility.

In January, 1951, she was admitted to the New York University-Bellevue Medical Center where surgical lengthening of her hamstrings and Achilles tendons was done on both sides. She was transferred to the Institute of Physical Medicine and Rehabilitation early in February, 1951.

Pertinent physical findings in February, 1951, were confined to her lower extremities. The legs were encased in plaster casts to the knees. The available muscle groups all showed spastic paresis. There were spotty and irregular areas of diminished sensation below the umbilicus as well as partial loss of vibratory and position sense. Bladder control was poor.

The training program consisted of daily baking under a heat lamp followed by stretching of her hip and knee flexors. After removal of her casts, this treatment was also applied to her heel cords. Since there was no involvement of her upper extremities, she was given progressive resistance exercises to increase strength of her arms and shoulders with a view toward crutch walking. She was then fitted with a double long leg brace and started ambulating between parallel bars. Bladder training was also instituted.

She became completely self-sufficient in the performance of activities of daily living within the scope of a wheel chair existence. Bladder control also improved. At this writing she is learning to walk with crutches, and is looking forward to returning home to her family soon.

CASE 2.—J. F. A., a 49-year-old white, single railroad clerk, began having bouts of blurred vision associated with numbness of his hands and progressive weakness of his legs, and partial loss of bladder control. His illness was diagnosed as multiple sclerosis in 1947. During the four years prior to his entry to the Institute of Physical Medicine and Rehabilitation, he became confined to a wheel chair, encountered increasing difficulties in caring for his daily needs, and rarely left his home.

On his entry, physical examination revealed a marked paresis of all muscle groups from his trunk down. There was some slight spasticity of his hip, knee and plantar flexors. There were large deficiencies shown in the Activity of Daily Living Test; his bladder control was poor, with intermittent occurrence of incontinence.

He was placed on a daily program consisting of heavy resistive exercises to increase strength of his arms and shoulders for crutch walking, stretching of the hip, knee and foot flexors, general conditioning and intensive training in activities of self-care including bladder training. He was fitted with long leg braces and a pelvic band and was started on ambulation. He was also provided with a light collapsible wheel chair with removable arm rests to facilitate moving from bed to wheel chair.

At the end of a three month period of training, he was completely self-sufficient in all activities of daily living, was able to get about with crutches with ease, using a swing-through type of gait. He could engage in activity for several hours without fear of urinary incontinence provided that he voided on schedule. He also manifested a desire to return to his former work.

He was discharged to his home after a three months' stay, and efforts were made through his local union to place him in some aspect of his former employment.

400 E. 34th St.

147
51

PROCUREMENT, ASSIGNMENT, AND UTILIZATION OF RESERVE MEDICAL OFFICERS

Howard A. Rusk, M.D., New York

Last year, when the Sessions on Military Medicine met in San Francisco, the questions of military medicine were academic to most physicians in the United States. While we were in session in San Francisco, however, this was dramatically changed by the headlines that Northern Korean Communists had invaded the South Korean Republic. Military medicine had once again become a matter of prime concern and responsibility for the American medical profession. Today the problem continues, and now once again within the relatively short span of 10 years our country girds for defense. Once again we must determine our most vital needs, measure our potential capacities, and allocate our resources to meet the critical needs of today and the years ahead. All of us feel the effects of the burgeoning national emergency as the mobilization of men and machines gets under way.

In his report of April 1 to the President, Defense Mobilizer Charles E. Wilson reported that 8% of our productive capacity is now devoted to defense, but by 1953 a peak of 20% is anticipated.[1] Military mobilization is moving at a faster pace. A year ago the strength of the armed forces was less than 1½ million; today it is nearly 3½ million.

In World War II the strength of the armed forces rose from less than a million in 1941 to a fighting force of 12 million in 1945, including a corp of medical officers which reached a peak of 60,000. Generally, there were from 5.6 to 6.2 physicians per 1,000 troop strength.[2] The armed forces, however, have constantly reduced their ratios over the past three years and are now operating at less than four physicians per 1,000 troop strength, a reduction of more than one-third. For this the armed forces certainly deserve the commendation not only of the medical profession but also of the public, which has benefited ultimately from these savings.

This reduction in the physician requirements of the armed forces has resulted from better planning, improved

Read before the Section on Miscellaneous Topics, Sessions on Military Medicine, at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

Chairman of the Health Resources Advisory Committee, Office of Defense Mobilization, and Professor and Chairman of the Department of Physical Medicine and Rehabilitation, New York University College of Medicine.

1. Building America's Might: Report to The President by the Director of Defense Mobilization, April 1, 1951, United States Office of Defense Mobilization.

2. Statement on S. 4029, in Hearing Before a Subcommittee of the Committee on Armed Services, United States Senate, Eighty-First Congress, Second Session.

utilization, unification of certain services, elimination of duplication, and many other factors. One of these factors has been the improved coordination between the services, which has resulted first from the establishment of the position of Director of Medical Services in the Office of the Secretary of Defense and the Armed Forces Medical Advisory Committee and now from the establishment of the Armed Forces Medical Policy Council. Under the present operating policies the needs for physicians, dentists, and veterinarians, as estimated by the three military departments, are first reviewed by the Armed Forces Medical Policy Council and then transmitted by the Department of Defense to the Health Resources Advisory Committee of the Office of Defense Mobilization for comments on the effect of such withdrawals on our civilian health economy.

As chairman of the Health Resources Advisory Committee, I would like to take this opportunity to briefly outline the role of this committee in the national mobilization. This committee is a new departure in government. Broadly, its aims are to evaluate and coordinate civilian and military demands upon our health resources and provide top mobilization officials with firsthand counsel in all aspects of health resources. During World War II comparable representation of health and medicine in the policy-making echelons did not exist. Almost everyone concerned has since recognized this weakness in the World War II mobilization, and on Aug. 5, 1950, soon after the outbreak of hostilities in Korea, at the suggestion of the President the Health Resources Advisory Committee was appointed as a consultant group to the National Security Resources Board. Subsequently, on April 30, 1951, the committee was transferred to the Office of Defense Mobilization, in line with the policy of centering certain operational activities in this agency.

Concurrently, an Interagency Health Resources Council was established, at which those persons responsible for the health policies and operations of the major Federal departments and agencies meet biweekly to discuss common problems. Illustrative of the activities of this council was the recent directive of the Department of Defense and the Veterans Administration providing that severely disabled service personnel whose disabilities seemed likely to preclude their return to active duty were to be transferred from military hospitals to the Veterans Administration. Among the effects of this policy, the implementation of which has been discussed at length at the Interagency Health Resources Council, has been the saving of physicians in critical categories of medical specialization by eliminating duplicate facilities and programs in the military forces and the Veterans Administration. Other typical items on the agenda of this group have been the utilization of foreign-trained physicians, civil defense, nurse recruitment, staffing of isolated facilities, and the effects of personnel freezes.

As reported in detail at the Annual Congress on Medical Education and Licensure in Chicago in February,[3] our committee has been deeply concerned with the problems of health manpower and is disturbed to find, as our studies indicate, that by 1954 the number of physicians available to the military and civilian populations will fall short by an estimated 22,000 of the number that may be needed. These estimates when established were based on the best possible data available, and, although the estimates have been questioned by some, later data has tended to confirm rather than alter their validity. For example, the 1954 estimated needs of the armed forces were based on the assumption of a possible military force of 5 million men. Recent congressional action indicates that in the extension of the Selective Service Law the ceiling on the armed forces will be established at 5 million.

More recent data also available to the committee from the Federal Civil Defense Administration has also verified the committee's original projected estimates that by 1954 the nation may need a total of 3,300 physicians for civil defense, 3,000 of whom are needed as reserves to meet catastrophes or epidemics; the remaining 300 are not full-time physicians in civil defense but rather represent the aggregate equivalent time that has to be spent by part-time physicians for civil defense.

The committee's estimate of the number of physicians required for the expanding industrial mobilization and for industrial medical requirements as a result of the industrial utilization of increased numbers of women, physically handicapped, and aged workers is substantially the same as the estimate of the Subcommittee on Manpower Conservation of the Committee on Industrial Health Defense of the Council on Industrial Health of the American Medical Association.[4] The committee's estimate of the projected additional need for physicians to man present vacancies in essential teaching positions in our medical schools has been declared by a group representing the Association of American Medical Colleges to be much too conservative.

I should like to point out that there is a definite difference of opinion between our committee and such groups as the Association of American Medical Colleges and the American Medical Association on the extent of the additional need for physicians caused by the national emergency. These differences, however, are primarily differences of degree, for, in most quarters, there is general agreement that the increased demands of mobilization are creating and will continue to create a greater demand for physicians than are or will be available to meet these demands. The medical needs for universal military training will place an added burden on our health resources.

Even though military ratios are being reduced, the number of physicians available to the civilian population will necessarily decline as military and industrial mobilization gains momentum. Our medical schools are increasing their enrollments, and, as compared with approximately 6,000 graduates annually at present, within the next five years they plan to graduate through normal increases in enrollment as many as 7,000 new physicians each year. This is heartening, and our medical schools are to be commended; the increase, however, is not enough to meet the sudden and urgent needs caused by mobilization.

The dentist situation is not quite as acute.[5] Today approximately 80,000 civilian dentists are actively engaged

3. Rusk, H. A.: Medicine, Mobilization and Manpower, J. A. M. A. **145**: 1256-1260 (April 21) 1951.

4. Progress Report of the Subcommittee on Manpower Conservation of the Committee on Industrial Health Defense of the Council on Industrial Health, American Medical Association, Chicago, Council on Industrial Health, American Medical Association, February 27, 1951.

V 14
1951

in their profession, and 2,900 are being graduated each year. As near as it is possible to estimate, 9,200 dentists over and above those now in sight for 1954 will be required to maintain the present level of civilian dental services, meet the special needs of industrial mobilization, the minimum needs of an adequate civil defense program, and the projected needs of the armed forces based on a ratio of two dentists per 1,000 troop strength.

In nursing, however, the situation is most critical.[6] The Joint Committee on Nursing in National Security of the Six National Nursing Organizations, after studying the problem, presented to our committee their estimate of 381,886 as the number of nurses needed to meet the minimum civilian requirements of the nation, excluding the military services.[7] Our committee has estimated that by 1954 the nation will need 379,500 graduate nurses to meet civilian requirements. If the armed forces mobilize 5 million men, another 25,000 nurses will be needed to meet military requirements, making a total of 404,500. It is interesting to note that although the two estimates of nursing needs were arrived at quite differently, they are very close together. Our committee's studies indicate that by 1954 the nation will be 49,200 nurses short of this goal. This estimate has assumed the staffing of new hospitals but no improvement in the existing hospital ratio of patients per nurse.

It is, of course, known full well why the demands for health manpower increase with the growth of the armed forces. Take the case of physicians, for example. One physician, on the average, has served approximately 850 civilians, but, because of dispersal, service industrial medical needs, dependent care, administration, and other factors, for every 1,000 physically qualified civilian men

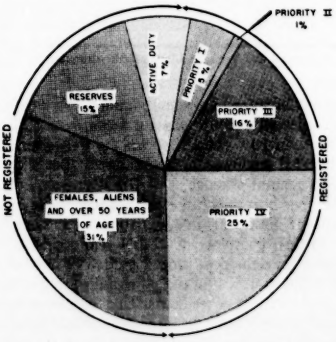


Fig. 1.—Selective Service classification Priority I physicians (April 30, 1951). Source: Selective Service System.

who enter the armed forces today, from three to four physicians are required. Hopefully, this ratio may be still further reduced in the future, but it can never even approximate the civilian ratio. Neither war nor mobilization for defense are economical ventures.

Our committee has been deeply concerned with the problems of utilization of health personnel, not only in its role as the Health Resources Advisory Committee to the Office of Defense Mobilization but also in its capacity as the National Advisory Committee to Selective Service. The National Advisory Committee was appointed by the President on Oct. 4, 1950, to advise Selective Service on the selection, under Public Law 779, of physicians, dentists, veterinarians, and allied specialists. Two days after taking office, this national committee appointed state committees to share in the responsibility of seeing that the calling of physicians and dentists registered under Public Law 779 would not disrupt essential community

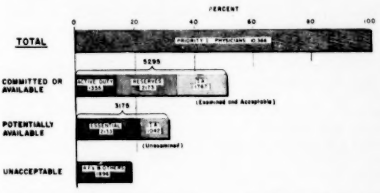


Fig. 2.—Per cent distribution of active physicians in the United States (based on an estimated 181,600 active physicians) according to priority status under Public Law 779 (April 30, 1951).

services. Membership of the state committees includes a physician, who acts as chairman, a dentist, and the state health officer. Each state committee appoints additional members and establishes subcommittees or regional committees as they are needed.

Under present arrangements with the armed forces, the names of all medical and dental reserve officers, excluding members of organized reserve units, being recalled to active duty are submitted prior to issuance of orders to the state advisory committee. If the officer being recalled is deemed essential to the health and welfare of his community, the state committee will ask that his recall be delayed. Although the final decision concerning the call of an essential reserve officer rests with the Secretary of Defense, to date this has presented no difficulties. It is particularly significant, I think, that by mutual agreement the military services for the first time in history have permitted a civilian group to be placed between them and their reserves and in the interest of total national welfare rely upon its advice and recommendations in calling their reserves to active duty.

Almost 90,000 physicians, roughly one-half of the active physicians in the United States, are registered in the four priority groups. The remaining half did not register because they were either already in the armed forces (on an active or inactive basis), women, aliens, or over 50. Of the total registrants, more than 10,000 are in Priority I; over 2,500 are in Priority II; 30,000 are in Priority III; and, by far the largest group, 45,000 are in Priority IV.

By the end of April, 10,366 physicians were registered in Priority I. At that time 1,355, or 13%, of the group had already gone on active duty in the armed forces; another 2,173, or 21%, had become reserve officers

5. Schoeny, L. J.: Dentistry, Mobilization and Manpower, J. Am. Dent. A. **42**: 548-557 (May) 1951.

6. Kuehn, R. P.: Nursepower in Mobilization, read before the Bureau of State Examiners for Nurses, Boston, May 4, 1951, Health Resources Advisory Committee, United States Office of Defense Mobilization.

7. Mobilization of Nurses for National Security: A Statement Prepared by the Joint Committee on Nursing in National Security of the Six National Nursing Organizations, Am. J. Nursing **51**: 78-79 (Feb.) 1951.

but had not yet been called to active duty, and 1,767, or 17%, had been placed in draft classification 1A and had been examined and found acceptable for military service. These groups together, 51% of the total Priority I physicians, were either already in the armed forces or readily available for military service. Another 1,042, or 10%, were 1A but not yet examined (many of these will become 4F's), and 2,133, or 21%, had been temporarily deferred as essential. Many of the men in these two groups were potential candidates for military service. The remaining 18% was made up of 4F's and others who would probably not become available. Thus, probably about 75% of the whole Priority I group can be expected to see military service. All men in Priority I who can be processed for military service will be called before Priority II is called on.

Since it may be of interest to know what effect Public Law 779 has had on the internship and residency programs at nonmilitary hospitals, I would like to present some of the information collected by the Health Resources Office of the Office of Defense Mobilization, in cooperation with almost 96% of the nonfederal and Veterans Administration hospitals.

Roughly 20% of all registrants under Public Law 779 were on the 1950 to 1951 house staffs of nonfederal and Veterans Administration hospitals as interns or residents. As a group they constitute about 50% of the registrants in Priorities I and II, 10% of those in Priority III, and 20% of those in Priority IV. The reports covered a total of 23,957 interns and residents on the medical house staffs of nonfederal and Veterans Administration hospitals during the 1950 to 1951 training year. Of this number, 1,926 had already entered active military service by Feb. 15, 1951 (many of them before the registration). A total of 2,883 did not register under Public Law 779 because they held reserve commissions at the time of registration, and 91 were on active duty but assigned to civilian hospitals. In Priority I were 3,480 of the remaining 19,057; 1,255 were in Priority II; 3,053 were in Priority III, and 7,785 were in Priority IV. Another 3,484 women, aliens, and men over 50 were not liable for registration. Some 1,283 of the 4,735 hospital registrants (about one out of every four) in Priorities I and II had accepted commissions between the time of registration and Feb. 15, 1951. These figures are summarized in Table 1. The 1,926 physicians on active duty as of Feb. 15th represent about 8% of the total 1950 to 1951 training year medical house staff. About 300 were men who had completed a first year internship, and about 1,600 were men taking more advanced training. Almost all specialties were represented among those called; but no one specialty group was cut more than 12%. Cuts of more than 10% were reported for only four specialties: internal medicine, obstetrics and gynecology, urology, and general practice.

Next year hospitals can expect to have their full complement of first-year interns, some reduction, about 15%, in their complement of first-year residents, and a much sharper reduction, probably 33% or more depending on military needs, in the potential supply of second, third, and fourth year residents. This forecast is based on the distribution of graduating classes according to priority groups. Classes graduating in 1947, 1948, and 1949 consist predominantly of men in Priority I, but classes graduating before 1947 as well as those graduating in 1951 and 1952 will be composed mostly of men in Priority IV. About 70% of the classes graduating in 1951 and 1952 are men who served during World War II and completed their medical education under the G. I. Bill on their return to civilian life.

In Public Law 779 congress has established a just and equitable system for calling the individual physician to military service. This law coupled with the existing agreement with the armed forces, which provides that reserve

TABLE 1.—*Military and Priority Status Under Public Law 779 of Medical Interns and Residents at Nonfederal and Veterans Administration Hospitals, 1950-1951, as of Feb. 15, 1951**

Status	Total	Commissioned	Not Commissioned
Grand total	23,957	8,779	15,178
Commissioned priority unspecified:			
On active duty	1,926	1,926	.....
On inactive duty †	2,883	2,883	.....
Civilian intern and resident program	91	91	.....
Registrants:			
Priority I	3,480	842	2,638
Priority II	1,255	396	859
Priority III	3,053	130	2,923
Priority IV	7,785	2,511	5,274
Not liable under P. L. 779			
Women, aliens, overage	3,484	.....	3,484

* Based on returns covering 96% of residents and interns in training at approved nonfederal and Veterans Administration hospitals.
† Men already in the reserves at time of registration.

TABLE 2.—*Military and Priority Status Under Public Law 779 of Medical Interns and Residents at Nonfederal and Veterans Administration Hospitals, by Year of Graduation, Feb. 15, 1951**

		Percentage Distribution							
			Priority Group				Prior Reserve Commission	On Active Duty	Women, Aliens, and Overage
Year of Graduation	Number	Total	I	II	III	IV			
1944 and prior	5,500	100	2	6	12	47	12	2	19
1945	2,400	100	4	9	4	57	17	2	7
1946	3,100	100	10	2	5	58	14	5	6
1947	2,000	100	41	5	11	6	9	17	11
1948	3,000	100	30	8	16	9	10	12	15
1949	3,100	100	23	6	19	11	9	11	21
1950	5,300	100	9	3	18	36	14	6	14

* Based on returns covering 96% of residents and interns in training at approved nonfederal and Veterans Administration hospitals.

V 14
1951

officers shall also be recalled in order of their priority, assures that all physicians eligible for military service will serve according to their past military service. Those deferred for training during World War II and those trained at the expense of the government are the first to serve; next in line are physicians with the least past military service.

In concluding, let me review some of the aspects of the national emergency which have special significance to those in the health field: 1. The armed forces have cut their physician requirement per 1,000 troop strength by more than one-third because of World War II and postwar experience. 2. For the first time in history we now have a mechanism, the Health Resources Advisory Committee, outside the armed forces to advise the Department of Defense on the effects of the withdrawal of physicians from the civilian population. 3. As a protection to individual communities, the national and state advisory boards have been set up to advise Selective Service about the calling of individual physicians. Through agreements with the armed forces, the state committees also recommend deferments for recalled reserve officers when they are essential to the health and welfare of their communities.

Compared with past experiences, all of these measures represent significant achievements. They will contribute immeasurably to an equitable allocation and the best utilization of our limited supply of health personnel. As we marshal our material, spiritual, financial, and human resources for whatever eventuality that may lie ahead, it is readily apparent that the most precious of these resources is manpower and that health is the most basic factor in the maximum realization of our manpower potential. The job of insuring adequate health services to both our civilian and military populations during this period of national emergency is a responsibility for all, but the major responsibility rests, as it always has, with the medical profession. We have never failed in the past —we shall not now.

325 E. 38th St.

EPIDEMIC OF HOMOLOGOUS SERUM HEPATITIS APPARENTLY CAUSED BY HUMAN THROMBIN

Mark Falcon Lesses, M.D., Boston
and
Milton W. Hamolsky, M.D., Malden, Mass.

147
51

The purpose of this article is to report a new and previously unsuspected cause of homologous serum hepatitis, namely, human thrombin.

The occurrence of homologous serum hepatitis following the use of whole blood,[1] plasma,[2] and irradiated plasma [3] has been reported by many authors. Homologous serum hepatitis is not only an established hazard of transfusion of blood and plasma but has also been shown to be transmitted by syringes and syringe needles used without adequate sterilization between patients.[4] In addition, tattooing with a common needle has been implicated as a means of transmission of the virus.[5] It has also occurred after the administration of convalescent measles and mumps serum and immunization against sandfly and yellow fever.[6] Transmission with amounts as little as 0.01 cc. of serum is possible, and it is probable that even smaller volumes may be infectious. The factor common to all modes of transmission is the transfer of infected human serum to susceptible recipients.

The use of human blood fractions and derivatives of these fractions has grown widely since World War II, when large quantities of pooled plasma were available as the starting point of blood fractionation. The clinical use of certain fractions has been extensive, particularly gamma globulin and albumin. Hepatitis has not been reported after use of either of these products, which are distributed in solution and, in the case of albumin, heat-treated. Occurrence of hepatitis has, however, been reported after injection of Fraction I, which is distributed in the dry state and which cannot be heat-treated without denaturation.[7]

One of the fractions of human plasma which has recently become commercially available is human thrombin. This product is derived from pooled plasma and is directly prepared from Cohn's Fraction III-2. After Seitz filtration it is dried from the frozen state for distribution. Clinically, thrombin has proved useful in controlling hemorrhage caused by extensive oozing, particularly in areas where suturing is not feasible, as in operations on the spinal cord or brain. The thrombin is dissolved in isotonic sodium chloride solution immediately before use and then used as such or placed in the interstices of a suitable matrix, e. g., absorbable gela-

From the Medical Service, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

1. (*a*) Lehane, D.; Kwantes, C. M. S.; Upward, M. G., and Thomson, D. R.: Homologous Serum Jaundice, Brit. M. J. **2**: 572-574, 1949. (*b*) McGraw, J. J., Jr.; Strumia, M. M., and Burns, E.: The Incidence of Posttransfusion Serum Hepatitis, Am. J. Clin. Path. **19**: 1004-1015, 1949. Robinson, J. W.; Twaddell, D. N., and Havens, W. P., Jr.: Homologous Serum Hepatitis, Ann. Int. Med. **32**: 1019-1027, 1950. (*c*) Ginzburg, L.; Sussman, L. N., and Auerhan, H.: Posttransfusion Viral Hepatitis as a Surgical Complication, Surg., Gynec. & Obst. **92**: 492-498, 1951.

2. Brightman, I. J., and Korns, R. F.: Homologous Serum Jaundice in Recipients of Pooled Plasma, J. A. M. A. **135**: 268-272 (Oct. 4) 1947.

3. Rosenthal, N.; Bassen, F. A., and Michael, S. R.: Probable Transmission of Viral Hepatitis by Ultraviolet-Irradiated Plasma, J. A. M. A. **144**: 224-226 (Sept. 16) 1950. Barnett, R. N.; Fox, R. A., and Snavely, J. G.: Hepatitis Following the Use of Irradiated Plasma, J. A. M. A. **144**: 226-228 (Sept. 16) 1950. James, G.; Korns, R. F., and Wright, A. W.: Homologous Serum Jaundice Associated with Irradiated Plasma, J. A. M. A. **144**: 228-230 (Sept. 16) 1950.

4. Capps, R. B.; Sborov, V., and Scheifley, C. H.: A Syringe-Transmitted Epidemic of Infectious Hepatitis: With Observations Regarding the Incidence and Nature of Infectious Donors, J. A. M. A. **136**: 819-824 (March 20) 1948. Sherwood, P. M.: An Outbreak of Syringe-Transmitted Hepatitis with Jaundice in Hospitalized Diabetic Patients, Ann. Int. Med. **33**: 380-396, 1950.

5. Roberts, R. H., and Still, H.: Homologous Serum Jaundice Transmitted by a Tattooing Needle, Canad. M. A. J. **62**: 75-78, 1950. Smith, B. F.: Occurrence of Hepatitis in Recently Tattooed Service Personnel, J. A. M. A. **144**: 1074-1076 (Nov. 25) 1950.

6. Runyan, J.; Wright, A. W., and Beebe, R. T.: Homologous Serum Jaundice: Report of Eight Fatal Cases, J. A. M. A. **144**: 1065-1068 (Nov. 25) 1950.

7. Janeway, C. A.: Clinical Use of Blood Derivatives, J. A. M. A. **138**: 859-865 (Nov. 20) 1948.

tin sponge ("gelfoam"). The manufacturer recommends storage of thrombin at refrigerator temperatures.

Prior to Aug. 23, 1950, bovine thrombin had been used as a hemostatic aid in operations at the Beth Israel Hospital. On that date and again on Oct. 20, 1950, two lots of human thrombin were purchased and made readily available in all operating rooms. It was used at operation in conjunction with absorbable gelatin sponge or a similar physical matrix to accelerate clotting over oozing surfaces. Employment of this material and its bovine predecessor during operation was not necessarily incorporated in operative notes, but the use of absorbable gelatin sponge was more regularly recorded.

were subjected to the same syringe and needle hazards strongly suggested that something other than blood transfusion was responsible. Finally, three of the six patients had had neurosurgical operations; this relatively high percentage of neurosurgical patients with hepatitis focused attention on technique and materials favored by the neurosurgeon, particularly the use of physical and chemical clotting agents, as exemplified by absorbable gelatin sponge and thrombin. The seventh patient with a diagnosis of homologous serum hepatitis re-entered the hospital on March 15, 1951, two-and-a-half months after cholecystectomy and almost seven months after the initial substitution of human for bovine thrombin. This

Data on Twenty-Two Patients with Postoperative Homologous Serum Hepatitis

		Operation				Initial Liver-Function Tests								
Age	Sex	Date	Type	Incubation Period, Days	Blood Transfusion	Bilirubin, Mg./100 Cc.	Thymol Turbidity, Units	Cephalin Flocculation	Alkaline Phosphatase Units	Prothrombin, %	Total Protein	Albumin, Gm./100 Cc.	Globulin, Gm./100 Cc.	Cholesterol	Cholesterol Esters
57	M	8/29/50	Abdominoperineal	94	Yes	17.0	27.3	3+	10.5	..	7.4	4.7	2.7	...	...
40	F	9/14/50	Laminectomy	126	Yes	22.1	53.6	2+	....	49	7.4	4.1	3.3	...	...
36	M	10/ 3/50	Closure ileal fistula	103	Yes	13.5	18.2	2+	....	15	6.1	4.1	2.0	234	92
32	F	11/21/50	Salpingo-oophorectomy	66	Yes	10.5	54.6	3+	4.8	60	7.0	3.9	3.1	241	147
67*	M	10/30/50	Laminectomy	94	Yes	7.5	....	1+	12.9	..	6.3	3.4	2.9	177	...
60	M	10/19/50	Cranlotomy	85	Yes	34.4	43	3+	7.8	15	7.0	4.2	2.8	232	76
55	M	11/28/50	Cholecystectomy	83	No	20.1	43.8	...	5.1	85	6.9	4.3	2.6	309	85
27	F	12/ 4/50	Cholecystectomy	107	Yes	12.9	93.8	4+	4.3	17.5	8.5	...	...	...	...
72	F	12/16/50	Cholecystectomy	94	No	16.5	100	...	8.6	..	7.2	3.7	3.5	...	...
50	M	12/ 7/50	Cranlotomy	82	No	13.5	6.0	2+	4.3	27.5	6.3	3.8	2.5	346	139
45	F	1/10/51	Cholecystectomy	80	No	22.3	52.8	4+	9.7	15.5	6.8	3.9	2.9	...	...
67	F	11/15/50	Cholecystectomy	133	No	4.5	60.9	...	5.9	..	...	...	...	...	...
22	M	1/12/51	Abdominoperineal	102	Yes	15.4	23	2+	6.2	58	...	...	...	309	126
30	F	1/16/51	Laminectomy	94	Yes	5.8	39.3	...	9.5	54	...	...	...	350	207
25	F	1/15/51	Cholecystectomy	98	Yes	14.8	37.0	...	8.2	28	...	...	...	256	97
32	M	1/16/51	Laminectomy	93	No	21.4	23.5	2+	5.7	94	...	...	...	253	113
52†	M	1/20/51	Laminectomy	100	Yes	10.9	....	3+	3.6	75	7.6	3.8	3.8	...	...
57	M	1/ 9/51	Excision cyst of mandible	136	No	3.8	16.4	1+	7.7	80	7.2	4.6	2.6	253	142
62	M	1/24/51	Rib resection	126	Yes	17.5	20.3	...	....	56	...	...	...	139	24
60	F	1/25/51	Cholecystectomy	104	No	15.7	27.9	4+	6.2	110	7.0	3.8	3.2	440	107
67	F	1/ 6/51	Cholecystectomy	137	No	19.7	28.2	...	5.6	66	7.4	4.3	3.1	...	...
71‡	M	1/20/51	Esophagectomy	136	Yes	8.2	31.0	3+	12.3	54	7.4	3.6	2.8	277	209

* This patient died; autopsy details are given in the body of the paper.

† Dr. Chester M. Jones of the Massachusetts General Hospital supplied follow-up information concerning this patient. The clinical course and laboratory data are compatible with the diagnosis of homologous serum hepatitis, although the possibility of obstructive jaundice has not been completely excluded at this time.

‡ The clinical course and laboratory data concerning this patient are consistent with the diagnosis of homologous serum hepatitis, although the possibility of liver metastases has not been fully excluded at this time.

The substitution of human for bovine thrombin passed unnoticed until the sudden occurrence of a number of cases of delayed postoperative hepatitis focused attention upon its possible causative role.

The first patient with postoperative hepatitis in this series re-entered the hospital on Dec. 4, 1950, four months after an abdominoperineal operation for a malignant rectal polyp. Since the patient had received three blood transfusions, in addition to widespread packing with absorbable gelatin sponge soaked in human thrombin, the cause of the jaundice was at first ascribed to serum hepatitis caused by whole blood. The occurrence of five subsequent cases of hepatitis within a two-month period represented a marked increase over a previously very low incidence of delayed posttransfusion jaundice. In addition, the lack of any cases occurring in patients who were not operated on but who received an equal number of transfusions from the same blood bank and was the first patient in this group who received no blood or plasma but on whom human thrombin was used extensively at the operative site. Within one month five more patients re-entered the hospital with jaundice, which occurred from 90 to 133 days after operation, and of these, four had received no blood or plasma or blood derivatives other than human thrombin. In these instances the surgeon made no specific mention in the operative note of the use of human thrombin but did note the use of absorbable gelatin sponge. This material has routinely been saturated with whatever thrombin was available from the operating-room shelf, and this consisted almost entirely of human thrombin during the period of the epidemic. Absorbable gelatin sponge itself is a synthetic material derived from gelatin and cannot be implicated as a source of hepatitis because of its origin and the fact that it is adequately sterilized in the manufacturing process.

V 14
1951

To date postoperative jaundice with the clinical and laboratory characteristics of serum hepatitis has developed in 22 patients (Table). The interval from use of the human thrombin until the appearance of symptoms has varied from 66 to 136 days, an incubation period entirely compatible with homologous serum hepatitis. During the epidemic period of 10 mo., no patients have re-entered the hospital with a similar clinical picture following hospitalization for any illness which did not require surgery, nor has there been any increased incidence of infectious hepatitis in the hospital population as a whole; thus, during the same time interval there were only four occurrences of infectious hepatitis. The patients with homologous serum hepatitis were both private and ward surgical patients, but there was no occurrence of homologous serum hepatitis in patients on the private or ward medical services. All medical and surgical floors, whether private or ward, are serviced by the same central supply room, blood bank, and clinical laboratories.

Of the 22 patients, 13 had one or more transfusions of whole blood and nine had none. No plasma was used in any patient in this series. Of the 13 patients receiving transfusions, none were given blood from common donors, a significant source for the multiple transmission of serum hepatitis.[1e] More than 98% of the donors utilized by the blood bank of the hospital during the epidemic period were nonprofessional, thus further decreasing the likelihood of evasive answers with regard to existent or pre-existent jaundice at the time of blood donation.

Of the 22 patients, almost one-third, or seven, had had neurosurgical operations (chiefly laminectomies), thus representing a very high incidence of hepatitis in a small group of patients. Hence, during the period of the epidemic, 1,232 operations were performed, of which 29 were neurosurgical (2.35% of the total); in seven, or 24%, of these 29 patients hepatitis developed. An additional eight patients had had cholecystectomy associated with excessive oozing of the gallbladder bed. The remaining seven patients had varied types of operations: Two had abdominoperineal resections, one a salpingectomy for ectopic pregnancy, one excision of a mandibular cyst, one a rib resection for tuberculous osteomyelitis, one closure of an ileal fistula, and one an esophagectomy.

The following is a report of the case of the one patient, out of the 22 in this series, who died.

REPORT OF A CASE

This patient (fifth entry in Table) was a 67-yr.-old man with a history of cholecystectomy 29 yr. previously and laminectomy for ruptured intervertebral disc one year previously. Because of persistence of back pain, he re-entered the Beth Israel Hospital on Oct. 21, 1950. A myelogram showed a block between the third and fourth lumbar vertebra, so a second laminectomy was performed on Oct. 30, 1950. At operation a large ruptured disc was found and removed. Absorbent gelatin sponge packs saturated with thrombin were used to control bleeding; in addition, two whole blood transfusions of 500 cc. each were given. The postoperative course was characterized by back pain, which was again investigated by a myelogram taken on Nov. 26, 1950. This disclosed a block at the fourth lumbar interspace, but no further procedures were performed. The patient was discharged on Dec. 3, 1950. He re-entered the hospital on Feb. 11, 1951, one week after noting dark urine, light-colored stools, and jaundiced skin. Examination disclosed a well-developed, well-nourished man with icterus of the skin and scleras. The heart was not enlarged, was fibrillating at a rate of 88, and was free of murmurs. The blood pressure was 144/90. The lungs were hyperresonant and free of abnormal breath sounds or rales. The liver was tender and palpable 3.0 cm. below the right costal margin. The upper border of dullness was percussed at the sixth rib. No other organs or masses were palpable in the abdomen. There were no other significant abnormalities found on examination.

The laboratory examination on admission showed the following facts: The urine revealed a specific gravity of 1.020, an acid reaction, a negative action for albumin, a 3 + reaction for bile, and a negative reaction for sediment. The hemogram showed 13.5 gm. of hemoglobin, a red blood cell count of 4,610,000 per cubic millimeter, and a white blood cell count of 5,800 per cubic millimeter, with 69% polymorphonuclear neutrophiles, 21% lymphocytes, and 10% monocytes. The stool was light yellow in color and was negative for occult blood by the guaiac test. Blood chemistry values (per 100 cc. of blood) were 85 mg. of blood sugar; 46 mg. of nonprotein nitrogen; 5 mg. of serum bilirubin direct and 7.5 mg. indirect; 177 mg. of cholesterol; 6.3 gm. of total protein, with 3.4 gm. of albumin and 2.9 gm. of globulin; 12.9 units of alkaline phosphatase; a 1 + reaction for cephalin flocculation; 43 units of serum amylase, and a positive reaction through 1:20 dilutions for urinary urobilinogen.

For 12 days the patient's course was satisfactory, when increasing icterus appeared, associated with worsening of the patient's condition. Ascites developed, followed by lethargy, weakness, and anorexia. The patient rapidly became comatose and died on the 15th hospital day.

Post-mortem examination disclosed the following significant findings: Twelve hundred cubic centimeters of odorless yellow fluid was found in the peritoneal cavity. Grossly the liver presented no abnormalities. Its surface was smooth and a mottled yellow in color. There were no abnormalities of the ducts, except for slight dilatation of the common duct without obstruction. On cut section the liver appeared homogeneous. The portal vein was free of thromboses or pylephlebitis.

On histological examination the liver showed massive necrosis and destruction, affecting primarily the central portion of the lobule, extending in some areas to the periphery. The architectural framework generally was still visible. There was an inflammatory reaction consisting predominantly of lymphocytes, plasma cells, and round cells, with occasional polymorphonuclears, eosinophiles, and frequent macrophages. All stages of degeneration could be seen with varying degrees of bile stasis, disappearance of nuclear detail, blurring of all cytoplasm, assumption of bizarre shapes, liquefaction, and disappearance. Occasionally rims of normally preserved liver cells were seen at the periphery of the lobule, but there was very little evidence of regeneration.

Other findings consisted of congestive pulmonary edema, bronchopneumonia, emphysema, toxic splenitis, and benign prostatic hypertrophy of residual prostatic tissue.

New cases of homologous serum hepatitis have continued to appear up to the time of writing this article, although all human thrombin was removed from the operating rooms on or about Feb. 6, 1951. Since the incubation period of homologous serum hepatitis may be as prolonged as 200 days, additional cases may be expected through July, 1951. Two lots of human thrombin were utilized during the period from Aug. 23, 1950, through about Feb. 6, 1951. The first lot was received Aug. 23, 1950, and the second on Oct. 20, 1950. One of these lots corresponded with the lot number of human thrombin utilized in another New England hospital, which has experienced a similar epidemic of postoperative homologous serum hepatitis,[8] apparently related to the use of human thrombin, and exhibiting a strikingly high incidence in patients who had undergone neurosurgical operations. A neighboring Boston hospital[9]

8. Dr. Joseph E. Porter of the Maine General Hospital supplied this information.

9. Dr. Carl W. Walter of the Peter Bent Brigham Hospital supplied this information.

also utilizing human thrombin had noted a similarly increased incidence of homologous serum hepatitis following the use of human thrombin in neurosurgical operations.

SUMMARY AND CONCLUSIONS

Twenty-two cases of homologous serum hepatitis, with one resulting in death, have occurred in a period of six months after operations in which thrombin derived from pooled human plasma was used for hemostasis. One-third of the patients with homologous serum hepatitis had undergone neurosurgical operations, although neurosurgical operations constituted only 2.3% of the total number of operations in this same period. No similar cases have occurred in the hospital population not subjected to operation, nor has there been a high hospital incidence of infectious hepatitis. Human thrombin is prepared by fractionation, freezing, and drying, but it is not subjected to viracidal techniques. Until these are available human thrombin should not be utilized therapeutically.

371 Commonwealth Ave. (Dr. Lesses).

REMISSIONS IN BRONCHIAL ASTHMA AND HYPERTROPHIC PULMONARY EMPHYSEMA

Alvan L. Barach, M.D., New York

Patients with bronchial asthma and the broncho-spastic type of chronic hypertrophic pulmonary emphysema occasionally manifest spontaneous remissions without discernible cause. Commonly, these periods of freedom from symptoms have followed unusual events in their lives, such as operations with ether anesthesia, sustained fever due to foreign protein reaction or infection (except virus caused), a critical emotional upheaval, or abrupt transfer to a new regimen involving the elimination of the accustomed medication. The purpose of this paper is to describe (1) the approach to remissive therapy, the aim of which is to initiate a prolonged period of freedom from wheezing, cough, and dyspnea, with utilization of the insights yielded by spontaneous remissions in patients, and (2) the measures for which a sound physiological argument may be presented.

In some of the early studies on inhalation therapy in patients with intractable bronchospasm it was surprising how often substantial benefit followed a physiologically directed program when administration of epinephrine and aminophylline was temporarily stopped. The change to a different pharmacological approach was required to substitute for the previously employed drugs in order to relieve dyspnea and anoxia, and ultimately to initiate a remission.[1] In recent years other measures [2] have been studied with the purpose of producing a longer and more complete symptom-free interval.

Read in part in the Clinical Session of the American Medical Association, Washington, D. C., Dec. 6, 1949.

From the Department of Medicine, Columbia University College of Physicians and Surgeons and Presbyterian Hospital.

1. (*a*) Barach, A. L.: Use of Helium in the Treatment of Asthma and Obstructive Lesions in Larynx and Trachea, Ann. Int. Med. **9**: 739, 1935; (*b*) Physiological Methods in the Diagnosis and Treatment of Asthma and Emphysema, ibid. **12**: 454, 1938; (*c*) Repeated Bronchial Relaxation in the Treatment of Intractable Asthma, J. Allergy **14**: 296, 1943. (*d*) Maytum, C. K.; Prickman, L. E., and Boothby, W. M.: Use of Helium and Oxygen in the Treatment of Severe Intractable Asthma, Proc. Staff Meet., Mayo Clin. **10**: 788, 1935. (*e*) Schwartz, A. L.: The Relief of Status Asthmaticus by Helium, J. Med. **19**: 122, 1938. (*f*) Segal, M. S.: Medical Progress: Inhalation Therapy, New England J. Med. **230**: 456, 1943. (*g*) Wickner, I.: Combined Helium and Epinephrine Therapy, Ann. Allergy **3**: 187 1945.

2. Barach, A. L.: Treatment of Intractable Asthma, J. Allergy **17**: 352, 1946. (*b*) Barach, A. L., and Garthwaite, B.: Physiologic and Antibiotic Therapy of Intractable Bronchial Asthma, Ann. Allergy **5**: 297, 1947. (*c*) Barach, A. L.: Advances in the Treatment of Diseases of the Chest, Cincinnati J. Med. **30**: 131, 1949.

The study of each asthmatic patient should naturally include the allergic work-up necessary to determine whether a specific hypersensitiveness can be effectively treated. Unfortunately, in many patients with intrinsic asthma, and in some with extrinsic asthma, treatment from a strictly allergic point of view does not prevent the evolution of a state of intractable bronchospasm in which progressive failure to respond to the usual bronchodilator medication results in a severe disturbance in bronchopulmonary function. The consequences of obstructive dyspnea include elevation of the intrapleural negative pressure during inspiration and a resultant congestion and edema of the walls of the smaller bronchi. When constriction of the bronchi continues unrelieved, the lungs become over-distended with air, and the diaphragm is flattened; this state of functional over-inflation of the alveoli persists until bronchospasm is terminated. In patients with organic chronic hypertrophic pulmonary emphysema the impaired elasticity of the lungs prevents the rise in intrapleural negative pressure during inspiration; during expiration the pressure in the intrapleural space tends to approach or rise above that of the atmosphere. In the presence of an exacerbation of bronchospasm, functional emphysema is added to the previous state of chronic alveolar distention.

Physiological therapy aims at the restoration to normal of an impaired function of the respiratory system. The procedures employed include: (1) continuous inhalation of oxygen, (2) intermittent inhalation of helium-oxygen mixtures, (3) pressure breathing, and (4) bronchodilator and bronchovasoconstrictor aerosols. In order to facilitate a remission the following measures have been employed: (1) withdrawal of epinephrine (adrenalin®), ephedrine, and aminophylline, i. e., medication previously employed; (2) substitution of other drugs to promote bronchial relaxation, such as meperidine (demerol®), paraldehyde, and ether; (3) fever therapy; (4) bronchial aspiration; (5) antibiotic therapy for an associated bronchial infection, and (6) treatment with cortisone or corticotropin (ACTH).

Intractable bronchial asthma was formerly characterized by refractoriness to epinephrine. After the introduction of intravenous administration of aminophylline

V 14
1951

by Efron [3] and Herrmann and Aynesworth [4] a high percentage of patients became symptom-free after one or two intravenous injections of aminophylline daily for four or five days in dosages of 0.25 to 0.5 gm. Caution should be exercised, however, in the administration of this drug, since death has occasionally occurred from too swift an injection. Eight minutes should be taken for administration of each 0.25 gm. intravenously. Rectal administration by a catheter and syringe of 0.6 gm. dissolved in 20 cc. of water is often equally effective and does not produce adverse side-effects on the circulation.[5] However, in many cases of severe asthma seen at the present time previous employment of large doses of aminophylline by mouth, rectally in solution, and by suppositories has rendered the patient partially refractory to this drug also.

For palliative therapy in patients who are not in an intractable asthmatic condition aminophylline in dosages of 0.2 to 0.3 gm. is the most satisfactory oral medication for the treatment of bronchospasm, provided it is given when the stomach is empty. Nausea, its chief adverse side-effect, is frequently relieved by ingestion of two teaspoonfuls of aluminum hydroxide.[6] Aminophylline is preferable to ephedrine for most patients, especially at night, since it is less likely to produce wakefulness, and since refractoriness to it generally develops slowly.

Combinations of aminophylline, ephedrine, and ethyl aminobenzoate (benzocaine), 0.15 gm., with or without a mild sedative, are frequently used for the morning dose, taken with a full glass of water on awakening. For medication on retiring it is generally better to omit ephedrine and include a quick-acting sedative (pentobarbital sodium) and a slow-acting drug such as phenobarbital.

In a study of 200 cases of bronchial asthma an attempt was made to appraise the value of palliative medication and procedures designed to achieve a full remission.[7]

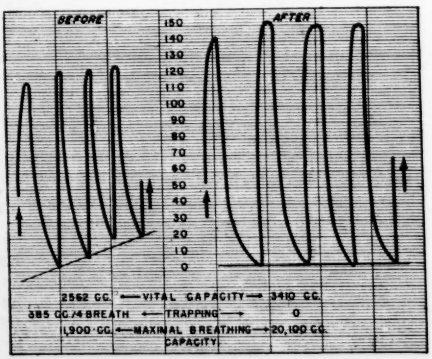


CHART 1.—Maximum breathing capacity (depth) and vital capacity before and after 0.3 gm. oral aminophylline.

The value of aminophylline by mouth was confirmed by respiratory-function tests of 50 patients.[8] In Chart 1 the response of a patient with bronchial asthma to ingestion of 0.3 gm. of aminophylline on arising is shown before dosage and one hour afterward. The rise in maximal breathing capacity (four deep breaths) from 11,900 cc. to 20,100 cc. is substantially greater than the rise of vital capacity from 2,562 cc. to 3,410 cc. Trapping of air, which was 385 cc. on arising, was conspicuously absent after ingestion of aminophylline.[8]

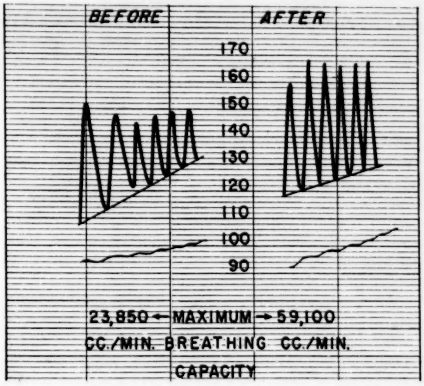


CHART 2.—Maximum breathing capacity before and after 0.5 cc. of 2.25% racemic epinephrine aerosol.

For immediate symptomatic relief of wheezing and cough in patients with bronchial asthma the inhalation of 1:100 epinephrine (or preferably 2.25% racemic epinephrine) by a fine particle-sized nebulizer is generally preferable to injection of 1:1,000 epinephrine or ephedrine by mouth. Nebulized epinephrine, like any other drug, should not be used to excess, but it has provided relief and comfort to many patients with few of the side-effects of systemic medication. No harmful effects from its use among properly instructed patients have been observed during the past 13 years. In Chart 2 a record of maximal deep breathing before and five minutes after inhalation of 2.25% racemic epinephrine revealed a rise in this ventilatory capacity from 23,850 to 59,100 cc.[9] The swiftness with which relief from dyspnea is obtained, combined with the prompt aid in expectoration of mucus has made it valuable in most cases of bronchospasm.[10]

3. Efron, B. G.; in Discussion on Kahn, J. S.: Status Asthmaticus, J. Allergy **8**: 163, 1938.

4. Herrmann, G., and Aynesworth, M. B.: Successful Treatment of Persistent Extreme Dyspnea: "Status Asthmaticus": Use of Theophylline Ethylene Diamine (Aminophylline, U. S. P.) Intravenously, J. Lab. & Clin. Med. **23**: 135, 1937.

5. Barach, A. L.: Rectal Instillation of Aminophylline in Intractable Asthma, J. A. M. A. **128**: 589 (June 23) 1945. Segal, M. S.; Levinson, L., and Beakey, J. F.: Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm, J. Clin. Invest. **28**: 1190-1949.

6. Nausea due to the local effect of aminophylline on the gastric mucous membrane appears to be effectively prevented by addition of ethyl aminobenzoate, 0.015 gm., to 0.2 gm. of aminophylline. Tablets containing 0.2 to 0.3 gm. of aminophylline with ethyl aminobenzoate and aluminum hydroxide, with and without ephedrine, 0.025 gm., were tested on 100 patients. Nausea was reported by only two subjects after repeated ingestion on an empty stomach, both on arising and on retiring. The medication for this study was provided by Irwin, Neisler & Co.

7. Barach, A. L.; Beck, G., and Bickerman, H. A.: Results of Antibiotic and Remissive Therapy in Bronchial Asthma and Pulmonary Emphysema, to be published.

8. Bickerman, H. A. and Beck, G.: Physiologic Therapy in Pulmonary Emphysema, Ann. Int. Med., to be published.

9. The study of aminophylline was aided by a grant from G. D. Searle & Co.

10. The nebulized epinephrine used in these studies was supplied by the Vaponefrin Co.

Bronchodilator medication in powered or "dust" form, such as isopropylarterenol is unnecessary and hazardous, since severe and alarming palpitation may result. Aminophylline dust is of little or no value and appears to be irritating.

When refractoriness to bronchodilator medication, i. e., aminophylline and ephedrine, has taken place it is necessary to curtail the use of these drugs in order to accomplish a remission and to restore the patient's sensitiveness to them. The procedures in inhalation therapy referred to may be employed to relieve dyspnea and to prevent anoxia, including the administration of oxygen-enriched air atmospheres and helium-oxygen mixtures. Pressure breathing, either with oxygen or helium-oxygen mixtures, may be employed in a weighted bellows apparatus in which a continuous pressure of 2 to 6 cm. is used.[11] The function of pressure breathing is not only to lower the pathologically elevated negative pressure during inspiration,[12] but also to maintain a wider lumen of the bronchial tree during expiration.[13]

My associates and I have found that the most suitable drug to substitute for the bronchodilator medication previously used is meperidine hydrochloride administered intramuscularly in doses of 50 to 75 mg. every six hours for a period of four or five days and then once or twice a day for two or three additional days. If excessive doses of barbiturate drugs are omitted, meperidine does not produce respiratory depression but accomplishes satisfactory bronchial relaxation in most cases. To patients with pulmonary emphysema it is advisable to give this drug in a similar dosage by mouth in order to avoid the possibility of addiction. In pulmonary emphysema dyspnea is apt to be of a chronic nature, and the temptation to addiction is greater when the drug is administered hypodermically. Potassium iodide is one of the most valuable drugs to combat intractable bronchial spasm and inadequate expectoration of viscid mucus, both in bronchial asthma and in pulmonary emphysema. The ingestion of 4 to 5 cc. of saturated solution of potassium iodide daily in divided doses for four days, followed by 1 to 2 cc. over an indefinite period, causes the secretion from the bronchi to become thinner, and it lessens the possibility of the formation of mucous plugs in the smaller bronchi. In some cases the addition of Fowler's solution, 0.2 cc. three times daily, has been of value although the rationale for its administration is obscure.

The barbiturates rarely serve a useful purpose in the treatment of bronchial asthma. However, use of both paraldehyde and ether may result in striking relief of bronchospasm and aid in the achievement of a remission. Paraldehyde may be given orally to an adult in a dosage of 6 to 12 cc. twice a day for three days, or rectally in somewhat larger doses adapted to the individual patient. To the average adult 120 cc. of ether may be administered rectally,[14] with an equal amount of oil, and the dose may be repeated two days later. The dosage may be figured on the basis of 0.8 to 0.9 cc. per pound of body weight. Precaution is always taken to place the patient on his side and to lower the head of the bed so that the tongue will not fall back into the throat. The patient should be observed for the duration of anesthesia.

In patients in whom a considerable amount of mucoid or mucopurulent sputum is present, the elimination of bronchial secretions may be facilitated by inhalation of nebulized 1% epinephrine, 2.25% racemic epinephrine, or mixtures of 0.3 to 0.5 cc. of epinephrine with 1.0 cc. of 1% phenylephrine (neo-synephrine*) hydrochloride, generally carried out three to four times daily. In patients who are refractory to hypodermic injections of epinephrine, local bronchodilatation and bronchovasoconstriction may take place, often followed by the expectoration of mucous plugs. After treatment with nebulized epinephrine, inhalations of helium with oxygen may be given, or the bronchodilator aerosol may be inhaled simultaneously with the helium-oxygen mixture by inserting the nebulizer into the mask.[15] When this procedure is followed, the high flow of the helium-oxygen mixture, i. e., 7 liters per minute, necessitates the addition of 2.0 cc. of isotonic sodium chloride solution to provide a gradual introduction of bronchodilator solutions. Under these conditions, 0.5 cc. of 2.25% racemic epinephrine, 1.0 cc. of 1% phenylephrine hydrochloride and 2.0 to 3.0 cc. of isotonic sodium chloride solution may be used. The results of continuous inhalation of bronchodilator and bronchovasoconstrictor aerosols on the vital capacity of the lungs, the expiratory and inspiratory velocity of air movement in asthma and pulmonary emphysema have been described.[15] The velocity of air movement increased at times from 30 to 100% of the control determination, more marked during expiration. These substances are nebulized by a flow of from 4 to 5 liters per minute of oxygen from a high-pressure cylinder, or by means of an electrically operated pump.

In a previous report of the measures outlined for the treatment of intractable bronchial spasm, 28 patients out of 54 admitted to the hospital for status asthmaticus showed improvement of marked degree, and 21, of moderate degree, or 91% significantly benefited.[1b] Of other measures of value in obtaining a satisfactory remission, fever therapy with a nontoxic typhoid vaccine stands out as a simple and safe method for many cases.[16] Administration of 5,000,000 organisms of typhoid vaccine intravenously, followed at three-day, four-day, or five-day intervals by injection of 10,000,000, 15,000,000 and 25,000,000 organisms may bring about a dramatic interruption of severe asthma in some patients. The dosage is varied according to the individual requirements

11. (*a*) Barach, A. L.: Physiologic Therapy in Respiratory Diseases, ed. 2, Philadelphia, J. B. Lippincott Company, 1948. (*b*) Bickerman, H. A., and Beck, G. T.: Pressure Breathing with Oxygen and Helium Oxygen in Pulmonary Edema and Obstructive Dyspnea, Bull. New York Acad. Med. **26**: 410, 1950.

12. Kernan, J. D., and Barach, A. L.: Rôle of Helium in Cases of Obstructive Lesions in the Trachea and Larynx, Arch. Otolaryng. **26**: 419 (Oct.) 1937.

13. Barach, A. L., and Swenson, P. C.: Effect of Breathing Gases Under Positive Pressure on Lumens of Small and Medium-Sized Bronchi, Arch. Int. Med. **63**: 946 (May) 1939.

14. Maytum, C. K.: Bronchial Asthma: Relief of Prolonged Attack by the Colonic Administration of Ether, M. Clin. North America **15**: 201, 1931.

15. Barach,[1b] Richards, D. W., Jr.; Barach, A. L., and Cromwell, H. A.: Use of Vaporized Bronchodilator Solutions in Asthma and Emphysema: A Continuous Inhalation Method for Severe Asthmatic States, Am. J. M. Sc. **199**: 225, 1940.

16. The typhoid vaccine employed is that made by the C. F. Kirk Co., New York. Another agent used is "pyromen," a purified pyrogenic material derived from Pseudomonas aeruginosa, manufactured by Baxter Laboratories, Inc., Morton Grove, Ill.

V 14
1951

of the patient, since a temperature of between 101 and 103 F. is considered necessary for a good therapeutic result. No instances of shock have been encountered with this vaccine, by my associates and me or by Dr. Irving Wright, how has used it over a period of 13 years.[17]

In some patients the inability to expectorate bronchial secretions presents a serious and at times grave problem. Bronchoscopic aspiration is in some instances a life-saving measure[18]; in others it may itself produce a prolonged remission, if carried out with deep ether anesthesia. At times the procedure has to be repeated in two or four days if a lasting result is to be obtained. Because patients with bronchial asthma are known to be sensitive to cocaine, the use of ether is considered preferable for anesthesia, accompanied with inhalation of a high concentration of oxygen.

A soft rubber tube has also been employed for bronchial aspiration.[19] In our cases my associates and I used rectal ether as the anesthetic, combined with a hypodermic injection of 100 mg. of meperidine hydrochloride or 1 to 2 mg. of dihydromorphinone (dilaudid®) hydrochloride. Bronchial aspiration is carried out in the patient's room and repeated in two or three days if necessary. In children the use of ipecac to promote vomiting is often of great usefulness, since mucus is expectorated from the bronchi effectively by the abdominal contractions which take place during emesis. Ipecac can also occasionally be used on adults.

Intravenous administration of 600 to 1,000 cc. of 5% alcohol in dextrose or 500 to 700 cc. of 10% alcohol in 5% dextrose daily for a period of five days, may promote bronchial relaxation, but it is generally not as effective as paraldehyde and ether.

Antibiotic therapy in bronchial asthma and pulmonary emphysema is indicated for the treatment of an associated chronic bronchitis or bronchiectasis, as well as for acute respiratory infections. When pyogenic infection has been demonstrated by the presence of pus cells in the sputum and by cultures, appropriate treatment may result in a long-sustained relief of dyspnea, wheezing and cough. Of 200 patients with bronchial asthma and pulmonary emphysema treated with penicillin, largely by inhalation, moderate to marked improvement took place in 97; in contrast, 46 of 50 patients having chronic bronchitis without bronchospasm manifested similar benefit, and 58 of 70 patients with bronchiectasis were significantly improved.[20]

It is evident from these results that persistence of bronchospasm due to allergic as well as infectious factors interferes with more complete relief of cough and wheezing. In fact, the physical impact of the mist results at times in an exacerbation of asthma. No true sensitization of the lungs has been observed as a consequence of aerosol therapy, but it is better to employ penicillin systemically in patients with bronchospasm unless bronchiectasis or extensive suppuration is present. Under the latter circumstances, previous inhalation of nebulized epinephrine is desirable. So-called dust or micronized penicillin is contraindicated in patients with asthmatic breathing since serious dyspnea may result. Improvement is at times marked, as emphasized by the report of Gay and Marriott,[21] after intramuscular injection of penicillin in cases in which active infection has been demonstrated.

Chronic bronchopulmonary infections, however, are admittedly resistant to treatment aimed at prolonged arrest or eradication of the disease. Since penicillin procaine administered systemically does not reach the sputum in effective concentrations, the results of intramuscular injection do not compare in effectiveness with those obtained by aerosol therapy in which high levels of penicillin are maintained in the lungs, bronchial walls and bronchial and nasal secretions.[22]

For long-continued therapy aerosol administration is more practical than is intramuscular injection of penicillin, especially in cases with extensive bronchiectasis and chronic sinusitis.[23] Since the effectiveness of aerosol antibiotic therapy has been clearly traced to the high concentrations of the drug in the lungs and bronchial secretions, the discovery by Jensen [24] of an ester of penicillin, benzylpenicillin diethylaminoethylester hydriodide, which is excreted in the lungs in unusually high degree, was promptly followed by its use in bronchopulmonary infections.[25] After intramuscular injection of 1,000,000 units of the hydriodide ester, Heathcote and Nassau [25] found effective concentrations in the sputum for a minimum period of six hours, i. e., 0.2 to 0.9 units per cubic centimeter of expectoration, and reported favorable clinical results in a small series of chronic nontuberculous suppurative pulmonary conditions. In current studies with the hydriodide ester my associates and I have confirmed the presence of penicillin in effective sputum concentrations in 15 patients under clinical treatment.[26] The expectoration of 10 patients, collected for 12 hours after injection of 1,000,000 units, revealed levels between 0.3 and 1.2 units per cubic centimeter of sputum.

17. Wright, I. S.: Vascular Diseases in Clinical Practice, Chicago, The Year Book Publishers, Inc., 1948.

18. Waldbott, G. L.: Emergencies in Allergist's Practice, J. A. M. A. **128**: 1205 (Aug. 25) 1945; Pollen Injections During the Hayfever Season, Tr. Am. Therap. Soc. **44**: 19, 1944.

19. Cardon, Leonard: Tracheobronchial Aspiration with a Urethral Catheter: Method of Treatment and Prevention of Asphyxial Hazard in Medical Diseases and Emergencies, J. A. M. A. **142**: 1039 (April 8) 1950.

20. (*a*) Footnotes 2[b] and 7. (*b*) Barach, A. L.; Silberstein, F.; Oppenheimer, E. T.; Hunter, T., and Soroka, M.: Inhalation of Penicillin Aerosol in Patients with Bronchial Asthma, Chronic Bronchitis, Bronchiectasis, and Lung Abscess: Preliminary Report, Ann. Int. Med. **22**: 485, 1945. (*c*) Barach, A. L., and Garthwaite, B.: Physiologic and Antibiotic (Penicillin) Therapy in Chronic Hypertrophic Pulmonary Emphysema, Dis. Chest **13**: 91, 1947. (*d*) Garthwaite, B., and Barach, A. L.: Penicillin Aerosol Therapy in Bronchiectasis, Lung Abscess and Chronic Bronchitis, Am. J. Med. **3**: 261, 1947.

21. Gay, L. N., and Marriott, H. J. L.: The Treatment of Infective Asthma with Penicillin in Beeswax and Oil, Tr. & Stud., Coll. Physicians, Philadelphia **15**: 91, 1947.

22. (*a*) Levine, E. R.: Inhalation Therapy in Chronic Bronchial Infections, Dis. Chest **13**: 295, 1947. (*b*) Barach, A. L.; Rumsey, C. C., Jr.; Soroka, M., and Rader, D.: A Simplified Technic of Treating Sinusitis with Penicillin Aerosol, with Description of Foot Pump for Economic Nebulization of Penicillin and Other Therapeutic Aerosols, New York J. Med. **47**: 1498, 1947. (*c*) Laurent, A. M.; McIlroy, A. P., and Hadley, F. P.: Penicillin and Streptomycin in Lungs and Blood Serum of Rats Following Inhalational and Intramuscular Administration, Proc. Soc. Exper. Biol. & Med. **68**: 213, 1948. (*d*) Segal, M. S.: The Management of the Patient with Severe Bronchial Asthma, Springfield, Ill., Charles C Thomas, Publisher, 1950.

23. A small, efficient, and inexpensive pump for nebulization of bronchodilator and antibiotic substances has been produced by Hugh A. Miller, 68 Sunset Road, Bay Shore, L. I.

24. Jensen, K. A.; Dragsted, P. J.; Møller, P., and Klaer, I: Undersøgelser af Penicillinpræparater og Doserings Måder II, Ugesk. laeger. **112**: 1043, 1950.

25. Heathcote, A. G. S., and Nassau, E.: Concentration of Penicillin in the Lungs: Effects of Two Penicillin Esters in Chronic Pulmonary Infections, Lancet **1**: 1255, 1951.

26. These results will be reported in full by A. L. Barach, H. Rose, H. A. Bickerman, and G. W. Melcher, Jr. The diethylaminoester of penicillin employed was supplied to us by Smith, Kline & French Laboratories, 1530 Spring Garden St., Philadelphia, under the name "neo-penil."

The clinical response of administration of 1,000,000 units daily for 8 to 14 days was observed in 15 cases of chronic bronchitis or bronchiectasis occurring in patients with pulmonary emphysema or bronchial asthma. In 10 patients the improvement was marked, with disappearance of pus, eradication of gram-positive organisms and substitution of gram-negative flora on culture and striking clinical benefit. In two patients who did not improve, penicillin aerosol therapy was effective in combatting an infection due to a resistant Staphylococcus aureus; in three others moderate improvement took place, enhanced by a subsequent course of chloramphenicol (chloromycetin®). No adverse reactions were encountered except in one patient in whom an exacerbation of asthma appeared to follow one injection. In two additional patients with advanced bronchiectasis and extensive suppuration due to Bacillus proteus, 2,000,000 units daily for 10 days was followed by a remarkable decrease in purulent secretion with a corresponding heightening of the patients' well-being. In another patient with an acute exacerbation of chronic sinusitis, treatment for eight days with 1,000,000 units daily resulted not only in clearing of the local symptoms but in the disappearance of a cervical node, 3 by 2 by 2 cm., which had persisted for three years prior to the present complaint, despite a comparable course of penicillin procaine and repeated courses of terramycin. Since this preparation may be given over long periods, its use for the treatment of chronic bronchopulmonary infections offers an encouraging prospect.

Since the broad spectrum antibiotics, aureomycin, chloramphenicol, and terramycin, were found to be so effective against both gram-positive and gram-negative bacteria,[27] as well as against virus pneumonia, my associates and I have conducted extensive trials of their use in acute and chronic bronchial infections in patients with bronchial asthma and pulmonary emphysema.[28]

Of 50 cases of chronic bronchitis in patients with pulmonary emphysema and bronchial asthma, marked or moderate improvement took place in 44 patients, following five to six days' administration of 2.0 gm. daily of either chloramphenicol, aureomycin or terramycin. The clinical benefit was prompt and conspicuous in 33, and paralleled by disappearance of pus cells and diminution of the number of infecting organisms in the expectoration. In 6 of 10 instances the sputum concentration of terramycin for four hours after ingestion of 0.5 gm. of terramycin was average 4 γ per cubic centimeter. A similar experiment with chloramphenicol gave levels approximately one-half those found with terramycin.

Although swiftness of improvement with the broad spectrum drugs is remarkable, the side-effects which accompany their prolonged use, generally required to accomplish arrest of infection, are the source of considerable discomfort and, at times, constitute menace to the health of the patient. In one patient with chronic bronchitis and pulmonary emphysema aureomycin was administered for 17 days without any adverse reaction, with total elimination of cough and expectoration and marked improvement in breathing, without recurrence for the past two years. However, nausea, frequent loose stools or a red inflamed pharynx occur as side-effects in variable degree in many patients. The superficial infection of the perianal region with Monilia has now been effectively prevented by instructing patients to wash the anus with water after each bowel movement instead of rubbing this region clean with toilet paper. The serious hazard of simultaneous elimination of gram-positive and gram-negative bacteria in chronic pulmonary disease was indicated by the development of active, persistent infection with Monilia in two, and with B. proteus in four, cases. Although gram-negative flora appear quickly after effective penicillin therapy, observed originally as a response to aerosol treatment,[20b] consistent improvement is generally observed despite their presence. Actual invasion, as reported by Weinstein [29] and others, is relatively rare, and can now generally be counteracted by intensive short courses of the broad spectrum antibiotics. Our present program is the use of penicillin as the mainstay of treatment for infections with gram-positive organisms and the employment of the broad spectrum antibiotics, especially chloramphenicol, for five days, when progression of improvement has been apparently limited by "penicillinase" formation by the gram-negative population. At the end of such a course penicillin treatment is begun again. With this regimen, invasion by resistant organisms for which no adequate therapy is available, such as B. proteus and Monilia, seems less likely to take place than when the broad spectrum antibiotics are employed for prolonged treatment of chronic pulmonary infections.

In the treatment of acute upper respiratory infections, the laryngotracheitis and sinusitis that follow the common cold, these newer antibiotics are generally of marked value when administered over a five-day period. Beginning about the third day of a coryza, each of the broad spectrum antibiotics is usually followed by prompt disappearance of pyogenic infection. Prevention of secondary development of asthmatic symptoms apparently takes place in some of these patients. Whether similar results will take place with the use of the new penicillin ester described above remains to be seen. Aerosol penicillin has appeared to be of special value in infections of the respiratory tract, a circumstance that suggests a special usefulness for a penicillin compound found in lung tissue and lymph nodes in a concentration at least five times higher than that obtained by comparable dosage of penicillin procaine.

The antihistamines have not been found of value in the treatment of the common cold or upper respiratory infections; in fact, excessive drying of the bronchial secretions has at times been responsible for severe, hacking cough in patients with asthma and chronic bronchitis.

The purpose of this discussion is not to outline all the measures that may be useful in the treatment of intract-

27. Collins, H. S.; Gocke, T. M., and Finland, M.: Aureomycin Therapy of Nonpneumococcic and Nontuberculous Bacterial and Pulmonary Infections, Arch. Int. Med. **84**: 875 (Dec.) 1949. McEntee, J. C.: Acute Laryngotracheobronchitis Treated with Chloromycetin, Lancet **2**: 910, 1949. King, E. Q., and others: Clinical Observations on Use of Terramycin Hydrochloride, J. A. M. A. **143**: 1 (May 6) 1950. Peterson, N. V., and Hadley, R. B.: Aureomycin: Its Use in Chronic and Acute Infections: Preliminary Report, Eye, Ear, Nose & Throat Month. **28**: 422, 1949.

28. Footnote 6. The broad spectrum antibiotics used in this study were supplied by Parke, Davis & Co., Joseph Campau Ave. at the River, Detroit; Charles Pfizer & Co., 11 Bartlett St., Brooklyn 6, N. Y., and Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

29. Weinstein, L.: The Spontaneous Occurrence of New Bacterial Infections During the Course of Treatment with Streptomycin or Penicillin, Am. J. M. Sc. **214**: 56, 1947.

V 14
1951

able asthma, but to present the point of view of deliberate insistence on the trial of one measure after another with the aim of securing a remission of significant degree. Admittedly, remissions may rarely take place spontaneously, but the procedures described tend to initiate a prompt and prolonged response.

Since pulmonary emphysema is generally characterized by persistent bronchospasm, the principles outlined here for the treatment of intractable bronchial asthma are frequently applicable to the patient with pulmonary emphysema. In addition to a program of this kind, the value of respiratory exercises has been reported.[30] The physiological training of the patient with pulmonary emphysema from the standpoint of diaphragmatic breathing has been described.[2c] It is well known that patients with pulmonary emphysema reveal little or no movement of the diaphragm on fluoroscopy. In advanced over-inflation of the lungs, the flattened diaphragm is of little use and the patient is forced to employ the neck and the intercostal muscles for thoracic expansion. However, in the usual ambulatory patient the maintenance of exclusively costal breathing is characteristic although generally not completely necessary. Thoracic breathing has become a habit in many patients with chronic hypertrophic pulmonary emphysema, and often in those with bronchial asthma as well. From observations on training patients of this type during recent years it has become evident to my associates and me that diaphragmatic breathing can be most easily taught to the patient when he is in the reclining position. Placing one hand on the chest and one hand on the abdomen, the patient is instructed to attempt to keep the chest quiet and lower the diaphragm as he inhales. With a little practice most patients are able to do this when lying down. With additional training diaphragmatic breathing may be learned in the sitting position and finally in the standing and walking position. The fact that diaphragmatic breathing can be done by patients in whom no movement of the diaphragm was observed on fluoroscopy was dramatically demonstrated by the use of electrophrenic respiration. In five patients with pulmonary emphysema, stimulation of the diaphragm by the electrophrenic resuscitator [31] was followed by excursion of the diaphragm and, in some cases, by a persistence of voluntary diaphragmatic movement for 6 to 10 breaths on the part of the patients themselves, after the current had been turned off.[32] This device is now used as part of the training program in patients with pulmonary emphysema, in order to make clear the kind of diaphragmatic movement desired.

When expiration is slowly carried out with the lips tightly pursed, the patients using physical effort to blow through a partially closed mouth, increased capacity for exercise without dyspnea is frequently acquired. This maneuver results in a back pressure that maintains a wider lumen in the bronchioles and increases the intra-abdominal pressure in expiration. It will be uniformly observed that wheezing rales in expiration will be diminished or eliminated when breathing is conducted in this manner. Exercise that formerly caused shortness of breath when the patient walked across a room may often be done without dyspnea with the training outlined here.

Manual elevation of the diaphragm by placing the hands under the ribs and pushing them upward and inward is also of considerable value in reducing the over-inflation of the lungs, especially when performed after inhalation of bronchodilator aerosols. From 200 cc. to 1,000 cc. of air may be eliminated by 10 compressions of the abdomen. The physiological advantages of raising the diaphragm by the use of an abdominal support have been repeatedly confirmed in clinical practice. If the physician presses the palm of his hand upward and inward on the lower abdomen, just above the pubis, he can demonstrate to the patient the value of a belt exerting similar pressure.

My associates and I have recently combined pneumoperitoneum with the use of the Burgess Gordon abdominal belt.[33] A smaller amount of air is used than in the treatment of pulmonary tuberculosis, i. e., just enough to raise the diaphragm about 2 in. (5.08 cm.). The relief of dyspnea is at times striking, especially in cases in which the venous pressure, reflecting the intrapleural pressure, falls after institution of pneumoperitoneum.

In the use of oxygen for patients with pulmonary emphysema a program of regulated increase of the oxygen concentration of the atmosphere was recommended to prevent the occasional development of coma.[34] In patients with preexisting anoxia due to pulmonary emphysema, at times abrupt administration of relatively high oxygen concentrations results in an unaccustomed high tissue-oxygen tension, with decrease of the pulmonary ventilation, increased carbon dioxide tension in the arterial blood and shift of the hydrogen-ion concentration to the acid side.[35] The response of patients with pulmonary emphysema to inhalation of oxygen is illustrated in Chart 3, in which the pulmonary ventilation during the inhalation of air and immediately following the application of 100% oxygen is recorded. It will be seen that a marked reduction in the volume of breathing took place, from 10.5 to 7.2 liters per minute, when oxygen was substituted for air. If a gradual increase of the oxygen concentration delivered to the patient is

30. Barach and Garthwaite.[2b] Barach.[2c] Livingstone, J. L.: Physical Exercises for Asthma, London, Research Council, Kings College, 1937. Hofbauer, L.: Pathologische Physiologie der Atmung, in Bethe, A.; Von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1925, vol. 2, p. 337. Saenger, M.: Ueber Asthma und seine Behandlung, Berlin, S. Karger, 1910. Cournand, A.; Brock, H. J.; Rappaport, I., and Richards, D. W. Jr.: Disturbance of Action of Respiratory Muscles as a Contributing Cause of Dyspnea, Arch. Int. Med. **57**: 1008 (May) 1936.

31. Sarnoff, S. J.; Hardenbergh, E., and Whittenberger, J. L.: Electrophrenic Respiration, Am. J. Physiol. **155**: 1, 1948.

32. This observation was made during a visit by Dr. John Sarnoff, who conducted the procedure in our clinic at Presbyterian Hospital.

33. (*a*) Beck, G.; Eastlake, C., Jr., and Barach, A. L.: Venous Pressure as a Guide to Pneumo-peritoneum Therapy in Pulmonary Emphysema, Dis. Chest, to be published. (*b*) Furman, R. H., and Callaway, J. J.: Artificial Pneumoperitoneum in the Treatment of Pulmonary Emphysema: Preliminary Report, Dis. Chest **18**:232, 1950. The Burgess Gordon Belt with two metal springs produces a comfortable and effective increase of pressure on the lower abdomen. It is made by George P. Pilling & Son Company, 3451 Walnut St., Philadelphia. Pressure should not be exerted above the umbilicus in patients with emphysema.

34. Footnote 1*b*. Footnote 20*c*.

35. (*a*) footnote 1*b*. (*b*) footnote 11*a*. (*c*) Barach, A. L., and Richards, D. W., Jr.: Effects of Treatment with Oxygen in Cardiac Failure, Arch. Int. Med. **48**: 325 (Aug.) 1931. (*d*) Richards, D. W., Jr., and Barach, A. L.: Prolonged Residence in High Oxygen Atmospheres: Effect on Normal Individuals and on Patients with Chronic Cardiac and Pulmonary Insufficiency, Quart. J. Med. **3**: 437, 1934. (*e*) Barach, A. L.: Impairment in Emotional Control Produced Both by Lowering and Raising the Oxygen Pressure in the Atmosphere, M. Clin. North America **28**: 704, 1944. (*f*) Comroe, J. H., Jr.; Bohnson, E. R., and Coates, E. O.: Mental Changes in Chronically Anoxemic Patients During Oxygen Therapy, J. A. M. A. **143**: 1044 (July 22) 1950. (*g*) Richards, D. W. Jr.: Symposium on Inhalational Therapy: Inhalational Therapy in Cardiac Diseases; Cardiac Failure, Bull. New York Acad. Med. **26**: 384, 1950.

carried out, such as 1 liter per minute through a nasal catheter for the first two days, and an increase of 1 liter per minute every other day, until 7 liters per minute is administered, this untoward state of affairs does not take place. The patient may then be given 40 to 50% oxygen by catheter, in a mask without rebreathing, such as the meter mask, or in an oxygen tent for one to three weeks, followed by a gradual reduction in the percentage of oxygen similar to that used in the early part of the treatment. Recovery of cardiac compensation and decrease in dyspnea may result, with some restoration of respiratory function which may continue for a period thereafter. The favorable response to oxygen treatment takes place even though the arterial carbon dioxide content increases from 50 to 100 vol. % or more, provided the pH does not shift toward acidity. The increase in carbon dioxide also represents a homeostatic mechanism, by which a greater concentration of carbon dioxide is exhaled per breath and is not merely interpreted as carbon dioxide toxicity. We have observed that when this regulated oxygen therapy program is carried out, neither delirium nor coma has occurred.[36]

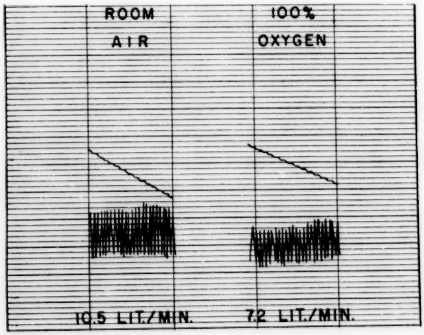


CHART 3.—Pulmonary ventilation in a patient with emphysema who was breathing air + 100% oxygen.

The beneficial effects of cortisone and corticotropin in the treatment of allergic conditions, and especially of status asthmaticus, have been recently described.[37]

The effects of 150 courses of corticotropin and cortisone administered to 68 patients with bronchial asthma and the bronchospastic type of pulmonary emphysema have been combined, since no significant difference in end-result was apparent in 75 cortisone, and 75 corticotropin, courses of treatment.[38] Complete freedom from asthmatic symptoms took place in 90, and partial freedom in 40, of the 150 courses. Excluding six patients in whom the remission lasted two to eight months, the average duration of benefit was 17 days. The results of treatment were considered to be of real value in 22 of the 68 patients, either because of prolonged relief due to the drug itself, or enhancement of moderate improvement subsequently by other remissive procedures. Exacerbation of severe asthma due to grass or ragweed pollen is, in my opinion, the ideal indication for short intensive courses of cortisone or corticotropin. The next most satisfactory response in this series took place in patients whose asthma had been well controlled until a viral respiratory infection precipitated intractable bronchospasm. This therapy seemed conspicuously not worth-while in the chronically severe asthma of the infectious or idiopathic type. High dosage and limited courses seemed to be important factors in initiating improvement and in the maintenance of long remissions without complications. Corticotropin appeared most effective when administered in a daily dosage of not less than 100 mg. for four or five days, cortisone, 300 mg. intramuscularly or 400 mg. orally for three or four days with diminishing dosage for a total of 10 days. With a regimen that included salt restriction, potassium chloride, 3 gm. daily, mercurial diuretics, and the usual precautions in selection of cases, no ill effects from this dosage were encountered.

SUMMARY

Termination of intractable bronchospasm can be induced by a variety of procedures in some patients with bronchial asthma who previously endured recurrent incapacitating cough and dyspnea. The purpose of remissive therapy is to induce an extended period of freedom from persistent asthma by the deliberate use of measures known to overcome refractoriness to bronchodilator drugs. Although the initial response to nebulized epinephrine, ephedrine and aminophylline is usually excellent, the frequent development of intractable bronchospasm requires a specific program to restore the patient's sensitiveness to small dosages of epinephrine or aminophylline.

Physiologically directed therapy involves the use of procedures which restore or maintain the function of the respiratory system. The pathology of the lungs and bronchi in many cases of bronchial asthma is largely reversible. Even in cases of hypertrophic pulmonary emphysema, in which a chronic, organic form of dyspnea appears to be present, favorable alterations in the pathological physiology of the disease may lead to marked improvement in respiratory function.

The patient with hypertrophic pulmonary emphysema requires special education in the use of mechanical aids to breathing, such as manual elevation of the diaphragm, low abdominal belts, training in diaphragmatic respiration and expiratory pressure breathing through pursed lips. The use of respiratory exercises in conjunction with other measures, including oxygen and bronchodilator aerosol therapy, may increase the ability of these patients to perform moderate exertion without excessive dyspnea.

36. Footnote 11a. Footnotes 35e and 2c. Barach, A. L.: Symposium on Inhalational Therapy: The Treatment of Anoxia in Clinical Medicine, Bull. New York Acad. Med. **26**: 370, 1950.

37. Howard, J. E.: Preliminary Report on the Results of ACTH in the Hypertensive States, Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950. Randolph, T. G., and Rollins, J. P.: Relief of Allergic Diseases by ACTH Therapy, Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950. Rose, B.: The Effect of ACTH on Eosinophilic Disease, Proceedings of the First ACTH Clinical Conference, Philadelphia, The Blakiston Company, 1950. Bordley, J. E., and others: Preliminary Observations on the Effect of Adrenocorticotropic Hormone (ACTH) in Allergic Diseases, Bull. Johns Hopkins Hosp. **85**: 396, 1949. Randolph, T. G., and Rollins, J. P.: The Effect of Cortisone in Bronchial Asthma, J. Allergy **21**: 288, 1950. Rosenberg, I. N.; Cleroux, A. P.; Raben, M. S.; Payne, R. W., and Astwood, E. B.: Clinical Evaluation of Corticotropin Therapy, A. M. A. Arch. Int. Med. **88**: 211 (Aug.) 1951. Segal, M. S., and Herschfus, J. A.: ACTH and Cortisone in the Management of the Hypersensitivities, with Particular Reference to Bronchial Asthma: A Review of Clinical and Laboratory Studies, Ann. Allergy **8**: 786, 1950.

38. Footnote 7. The Cortisone used in this study was furnished by Merck & Co., Inc., Rahway, N. J.

V 14
1951

Miscellaneous measures that frequently result in a general modification of hypersensitiveness include fever therapy, anesthesia with ether or paraldehyde, and the use of drugs such as meperidine (demerol®) and iodides. Bronchial aspiration with the bronchoscope or soft rubber tubes, carried out under ether anesthesia, may eliminate obstructing mucous plugs from the bronchial airway and produce a prolonged remission.

An analysis of procedures recently studied include the following data:

1. The administration of 150 courses of corticotropin (ACTH) and cortisone to 68 patients was followed by a full or partial remission in 130 instances. The average duration of benefit was 17 days, excluding six cases with remission of two to eight months. The best results were obtained in patients in whom an exacerbation of asthma was precipitated by pollen or respiratory infection.

2. Antibiotic therapy frequently produced significant benefit in patients with an associated bronchitis or bronchiectasis, i. e., 97 of 200 were treated with penicillin; 44 of 50 were given aureomycin, chloramphenicol (chloromycetin®) or terramycin, and 15 were treated with a diethylaminoethyl ester of penicillin. The broad spectrum antibiotics were considered highly valuable in acute respiratory infections and, for brief periods after prolonged penicillin therapy, in chronic bronchopulmonary disease, since they served the purpose of eliminating penicillinase or, rarely, infection due to the secondary growth of gram-negative bacteria. Simultaneous eradication of gram-negative and gram-positive bacteria was followed in certain cases by invasion with such highly resistant organisms as Bacillus proteus and Monilia. Penicillin therapy, therefore, was regarded as the mainstay of treatment in chronic respiratory infection due to gram-positive bacteria, and the broad spectrum antibiotics were used in an in-between course when indicated. Since the diethylaminoethyl ester of penicillin was found in the sputum in effective concentrations after intramuscular injection, an additional agent for the management of respiratory tract infection is described.

929 Park Ave.

RED BLOOD CELL SUSPENSION TRANSFUSIONS

Donald W. Smith, M.D.
and
John Elliott, Sc.D., Miami, Fla.

147
951

Improved techniques and better understanding of indications for blood transfusions have brought a new era of transfusion therapy. Technical advances culminating in the aseptic collection of blood into a sterile closed system [1] containing maximally effective red blood cell preserving solutions have greatly simplified the procedure of blood transfusion.

The immediate availability of blood at blood banks has led to an increased use of blood. This year it is estimated that 3 million transfusions will be given for routine civilian needs. Obviously, there must be no waste of blood.

Blood has two major components: plasma and red blood cells. Often there are contraindications to the use of both components simultaneously, and the indication is for the transfusion of a single component. The proper use of the major components of blood, together or separately as indicated, will insure that blood will not be wasted and that the estimated 3 million or more transfusions required during the year will be accomplished.

A clearer understanding of the significance of blood volume in disease, of the altered physiology in anemia and shock, and of the disturbed physiology in medical disease makes it possible to intelligently use whole blood or one or the other of the major blood components.

Although indications for the use of plasma,[2] clearly established by research and particularly by the experience during World War II, are well known, red blood cell suspension transfusions have been neglected. Rous and Turner [3] (1916) showed that red blood cells could be stored outside the body in suitable preservative solutions, and two years later Oswald Robertson [4] transfused red blood cells suspended in this preservative. Research has brought about improvements in transfusion techniques, including the preparation of red blood cell suspensions at modern blood banks. This, together with a better understanding of the indications for red blood cells, has focused attention on this component of whole blood.

Cell-suspension transfusions were first issued from the blood bank of Dade County in 1941. More than 75,000 transfusions, with a present average of 28,000 transfusions a year, have been prepared at the blood bank. Of this number, approximately 15% are given as suspensions of red blood cells, and an equal number as plasma. The discussion of the indications for cell-suspension transfusions is based on the experience of the blood bank of Dade County.

INDICATIONS FOR RED BLOOD CELL SUSPENSION TRANSFUSIONS

The principal indications for cell-suspension transfusions are (1) uncomplicated anemia (iron deficiency), (2) anemia in cardiac disease, hypertension, or nephritis, where an increase in blood volume is definitely contraindicated, (3) anemia in cases in which it is necessary to rapidly and effectively increase the oxygen carrying

1. Elliott, J.: A Preliminary Report of a New Method of Blood Transfusion, South. Med. & Surg. **98**: 643-645, 1936. Elliott, J., and Nesset, N.: A Report on the Use of a Perfected Evacuated Unit for Blood Transfusion, South. Med. & Surg. **102**: 203-206, 1940.

2. Tatum, W. L.; Elliott, J., and Nesset, N.: A Technique for the Preparation of a Substitute for Whole Blood Adaptable for Use During War Conditions, Mil. Surgeon **85**: 481-489, 1939. Elliott, J.; Busby, G. F., and Tatum, W. L.: Some Factors and Observations on Preparation and Preservation of Diluted Plasma, J. A. M. A. **115**: 1006-1008 (Sept. 21) 1940. Elliott, J.: Blood Plasma, Mil. Surgeon **88**: 121-125, 1941.

3. Rous, P., and Turner, J. R.: The Preservation of Living Red Blood Cells in Vitro, J. Exper. Med. **23**: 219-222, 1916.

4. Robertson, O. H.: Transfusion with Preserved Blood Cells, Brit. J. Surg. **1**: 691-695, 1918.

capacity of the blood, and (4) preparation of anemic patients for surgery when their blood volume is normal.

Shock.—Shock is discussed first in order to emphasize the ineffectiveness of red blood cell suspension transfusions. Red blood cell suspensions do not effectively increase the blood volume. This kind of transfusion must never be used in the treatment of shock, since the osmotic pressure of this preparation is only that of the suspending crystalloid media. There is no significant retention in the vascular tree of the fluid injected with red blood cells. Since the capillaries are freely permeable to water, electrolytes, and crystalloids, a Donnan's equilibrium will shortly be set up and 75% of the suspending fluid will pass into the tissues through the capillaries and only 25% will be retained in the vascular tree until it is lost from the circulation through the kidneys, skin, and expired air.

Only colloids are capable of holding fluids in the vascular tree. Red blood cells have no osmotic functions capable of increasing the effective blood volume. They may be considered closed enzyme systems which contribute to the total blood volume and the viscosity of the blood. They have no part in maintaining the effective blood volume. Therefore, the transfusion of red blood cell suspensions will not be a factor in increasing blood pressure and circulation.

There is, however, a use for red blood cells in persons who have been effectively treated for shock by transfusions of blood plasma. After the blood volume has been restored in these patients, red blood cells may be given, if necessary, to correct defects in the hemoglobin and red blood cell count. In many instances a neurogenic type of shock develops in persons who have lost 10% or less of their blood volume by hemorrhage. In these individuals it is unlikely that red blood cells will be required after the blood volume has been restored with plasma. The use of whole blood in treating shock in such cases may waste the red cell components. In the treatment of shock the plasma proteins are all-important in restoring effective blood volume. The proper use of red blood cell suspensions in patients requiring these elements of the blood must be on the basis of need rather than on the use of whole blood as a routine therapeutic procedure for shock.

Elective Surgery.—The preparation of anemic patients for elective surgery requires the restoration of hemoglobin in addition to other therapy. Patients who have a normal blood volume should be treated with red blood cell suspension transfusions, since often a single transfusion procedure may restore their hemoglobin and red blood cell deficiency to the desired level. In cases of marked anemia, as a prophylactic measure against shock, the last one or two units required should be given as whole blood just before or during the operation in order to maintain the blood volume and circulation at an optimal level. Transfusion of whole blood at the time of operation will serve two purposes: (1) to correct the remaining anemia, and (2) to maintain blood volume. In addition this prevents or minimizes the waste of blood.

Chronic Hemorrhage and Chronic Anemia.—Transfusions are indicated in chronic hemorrhage associated with a normal blood volume, in iron deficiency anemia, nutritional anemia, anemia of pregnancy uncomplicated by toxemia, and in certain other blood dyscrasias. When whole blood is used, the plasma element is wasted. Even in nutritional anemia the small amount of protein transfused as whole blood is not therapeutically effective. The protein requirement of such patients can best be supplied in the diet or by the infusion of amino-acid preparations. For example, the daily protein requirement of a normal individual is 45 to 70 gm., which in disease may be increased to 150 gm. or more.[5] The plasma of 500 cc. of blood yields approximately 19 gm. of protein.[6] It would be necessary, therefore, to give the plasma of 1,500 to 2,000 cc. of whole blood to supply the daily protein requirements of a normal individual. The same amount of protein can be obtained readily from 1,000 to 2,000 cc. of 5% amino acid or 50 to 150 gm. of protein in the diet. The maintenance of protein in a patient with whole blood is wasteful and expensive.

Pediatric Uses.—The size of the pediatric patient and the degree of accessibility of his veins limits the volume of substances that can be given intravenously. In these patients red blood cell suspensions are better tolerated and may be given in larger volume than whole blood. Red blood cell suspensions are found to be particularly useful in treating blood dyscrasias of all types associated with normal blood volumes. Fewer transfusions need be given, and few if any overload reactions will be encountered. It must be borne in mind, however, that whole blood must be used for exsanguination transfusions in erythroblastosis fetalis. In the treatment of dehydration resulting from infant diarrhea, and in severe infection where shock is present or is impending, whole blood or plasma must be used to maintain effective blood volume or to restore a lowered one.

Cardiac Patients.—The majority of cardiac patients, and certainly those undergoing surgery, do not tolerate sudden increases in the effective blood volume, and they must be guarded against overload transfusion reaction. Since plasma increases the effective blood volume, while blood cells, as previously mentioned, do not increase the effective blood volume but add only to viscosity of the blood, red blood cell suspensions are a safe and effective method of correcting the anemia in these patients.

Patients who have anemia associated with cardiac disease in which increased intake of sodium chloride is contraindicated may be treated with red blood cell suspensions to restore hemoglobin and red blood cell count without increasing the body sodium chloride. Cell suspensions contain relatively small amounts of sodium chloride, approximately 4 gm. NaCl per liter, compared with 9 gm. per 1,000 cc. of whole blood.

5. McKenzie, B. W., and Elliott, J.: The Serum Proteins in Pyogenic Infections, South. Med. & Surg. **97**: 7-10, 1935.

6. Elliott, J., and Marsh, F. B.: Preparations and Therapeutic Use of Liquid and Frozen Plasma and Serum, in Mudd, S., and Thalheimer, W.: Blood Substitute and Blood Transfusions, Springfield, Ill., Charles C Thomas, Publisher, 1942, chap. 3.

V 14
1951

METHODS

Preparation of Red Cell Suspension.—In the experience of the blood bank of Dade County, approximately one in five to 10 patients will require only the red blood cell components of whole blood. Accordingly, blood is collected from healthy donors of the proper blood group and Rh type, into sterile evacuated bottles containing 50 cc. of 4% sodium citrate. The blood is allowed to stand at a temperature of 6 to 10 C for 12 to 24 hours and is then spun in a centrifuge at 2,000 rpm for one hour. After centrifugation, the blood should remain in the refrigerator another 24 hours to permit the cells to completely settle out of the supernatant plasma.

The plasma is removed aseptically, using a sterile evacuated bottle. Immediately after removing the plasma, the opening through the free hole in the rubber stopper must be closed. A sterile "Diack sterilization control" tube is used for this purpose at the blood bank of Dade County.

Packed red cells are stored without dilution, and the maximum storage period of five days (from the date of collection) is marked on the bottle label. Packed red cells should be resuspended only on the day of use. Alserver's solution is the preferred resuspending fluid, since it contains but half of the sodium citrate as the same volume of acid-citrate-dextrose. The latter solution, however, may be used with satisfactory results.

The dating period of blood collected in acid-citrate-dextrose (ACD) solution allows a storage period up to 21 days, as this solution preserves whole blood more effectively than blood collected in sodium citrate. Cell suspensions may be prepared from blood collected in acid-citrate-dextrose which has been stored up to 21 days. The plasma may be removed from such whole blood without centrifugation. Sufficient plasma will be present in the uncentrifuged cell pack to permit satisfactory administration without further dilution.

At the blood bank it is considered that cell preparations are better if drawn in sodium citrate rather than acid-citrate-dextrose for the following reasons:

1. Because of the lesser volume of the diluent in the bottle, 75 cc. more of whole blood may be withdrawn from the donor, yielding more cells in the resulting cell pack.

2. Plasma removed from the cell pack is likewise of greater volume and has better keeping qualities insofar as the precipitation of fibrin is concerned.

When excessive quantities of fluid or sodium chloride are undesirable for the patient, the centrifuged cell pack may be resuspended in quantity sufficient to permit easy administration. It is not necessary to resuspend the cell pack to the 500 cc. mark on the bottle. Alserver's solution and acid-citrate-dextrose solution contain about 0.4 gm. of sodium chloride per 100 cc. and therefore both may be considered salt poor diluents.

DOSE OF BLOOD

Blood is usually drawn into bottles with a capacity of 500 cc. of whole blood. This is the amount which may be safely withdrawn from the doner. It is not the dose of blood.

The dose of blood or blood component is that amount necessary to restore and maintain normal blood volume and hemoglobin. This may require replacement of a large proportion of the patient's estimated blood volume. In an adult it seldom if ever is less than 500 cc.

The theory that smaller doses of blood stimulate red blood cell maturation has not been confirmed in our experience. The observed delay in the increase in red blood cell count following transfusion is most likely based on changes in blood volume when whole blood is transfused. For example, a patient weighing 100 lb. (45.4 kg.) with a normal blood volume of 4,000 cc. experiences a 12.5% increase in blood volume immediately following the transfusion of 500 cc. of whole blood. If the plasma proteins are increased by the transfusion, there will be an increase in blood volume due to the ability of the proteins, by increased osmotic pressure, to pull fluid into the vascular tree. As this increased blood volume contracts to normal, a relative rise in red blood cell count may be observed. The final adjustment of blood volume and red blood cell concentration may not be accomplished for 24 hours or longer. Fluctuations in blood volume in a bleeding patient, for example, may be so great that no significant rise may be observed in the red blood cell count following transfusion.

In calculating the dose of blood or blood components to be transfused, consideration must be given to the patient's estimated normal blood volume and the status of the patient's cardiovascular and renal systems.

Calculation of Blood Cell Needs

Statistics:

Normal values

8% of body weight is whole blood

Using 500 cc. = 1 lb. (0.5 kg.)

then

8% of 500 = 40 cc. (amount of blood per pound of body weight)

1 donor unit of whole blood or resuspended cells = 500 cc.

Example:

Patient's weight = 100 lb. (45.4 kg.)

Estimated normal blood volume = 40 cc. × 100 = 4,000 cc.

Ratio of donor unit to patient's estimated blood volume $= \frac{500 \text{ cc.}}{4{,}000 \text{ cc.}} = 12.5\%$

Rise in red cell count expected from 1 donor unit transfused = 5,000,000 cu. mm. × 12.5% = 625,000 cells per cu. mm.

or

Rise in hemoglobin expected from 1 donor unit transfused = 15 gm. × 12.5% = 1.87 gm. of hemoglobin

or

100 × 12.5 = 12.5% hemoglobin

If patient's actual red blood cell count = 2,000,000 per cu. mm.

If desired level = 4,500,000 per cu. mm.

Deficit cells = 2,500,000 per cu. mm.

Deficit $= \frac{2{,}500{,}000}{625{,}000} = 4$ donor units (2,000 cc.) required to restore count to 4,500,000

or

If patients hemoglobin is 40% and the desired level is 90%, then the deficit is 50% hemoglobin

Then: $\frac{\text{Deficit}}{\text{Increase per unit}} = \frac{50\%}{12.5\%} = 4$ donor units (2,000 cc.) required to restore hemoglobin to 90%

Method of Calculation.—Normally 7.5 to 8% of the body weight is blood. For practical purposes 8% is used to calculate the normal blood volume, and for practical purposes one pound is considered equivalent to 500 cc. (Table).

An individual weighing 100 lb. (45.4 kg.) has a blood volume of 4,000 cc., since 8% of 100 lb. is 8 lb. and eight times 500 cc. equals 4,000 cc. On this basis, 40 cc. per pound of body weight may be used as the factor for the rapid calculation of the estimated normal blood volume. In determining the dose of blood it is necessary first to calculate the percentage ratio between the donor unit, 500 cc., and the total estimated blood volume of the patient. In a patient weighing 100 lb. this may be accomplished by dividing 500 cc. by 4,000 cc. Each 500 cc. then equals 12.5% or one-eighth of the patient's estimated blood volume. Normal blood cell count or hemoglobin multipled by this percentage gives the increase in red count or hemoglobin to be expected from the transfusion of 500 cc. of whole blood

or resuspended red blood cells. Again in the 100-lb. patient a single 500 cc. transfusion of normal blood should increase the patient's red blood cells by approximately 625,000 cells per cubic millimeter (5 million times 12.5% equals 625,000). The transfusion of blood with a normal hemoglobin (100%) should increase the patient's hemoglobin content by 12.5%; or expressed in grams, a normal hemoglobin of 15 gm. multiplied by 12.5% gives 1.87 gm. rise in hemoglobin following a 500 cc. transfusion of blood.

In determining the total amount of blood required to bring the red cell count or hemoglobin to the desired level, the differences between the actual and desired red cell blood count or hemoglobin is calculated. This difference is divided by the estimated increase from a single 500 cc. unit of blood in order to determine the number of units required to attain the desired level. For example, a patient weighing 100 lb. having an estimated blood volume of 4,000 cc. will have a 12.5% increase in red blood cells or hemoglobin by the transfusion of 500 cc. of whole blood. With an actual red blood cell count of 2 million and a desired count of 4 million there would be a deficiency of 2 million red blood cells. This figure divided by 625,000 indicates that 3.2 units or 1,700 cc. of whole blood or cell suspension is required. Likewise, using hemoglobin as the guide for therapy, if the hemoglobin of this patient is 40% and the desired level is 80%, a deficiency of 40% hemoglobin exists. This figure (40) divided by 12.5% (the increment obtained with one 500 cc. transfusion) results in the requirement of 3.2 units (1,700 cc. of whole blood) to restore the hemoglobin to 80%.

The experience of the blood bank in the use of this simplified formula has resulted in excellent agreement between the calculated dose and the results obtained when that amount is transfused into patients.

REPORT OF A CASE

A 200-lb. (90.7 kg.) patient from South America was admitted to Jackson Memorial Hospital at 5:00 p. m. with a bleeding peptic ulcer. He had been given four transfusions of whole blood for shock, and had a red blood cell count of 2 million, or a three-fifths deficit, on admission. His estimated blood volume, determined by multiplying his weight of 200 by 40 (cc. per pound), was 8,000 cc. Therefore, he needed three-fifths of 8,000 cc., or the cells from approximately 4,800 cc., of blood to bring him to a red blood count between 4½ and 5 million. It was considered that operation must be undertaken on this patient, so he was given the cells of 4 pints (1.9 L.) of blood, resuspended to the original 2,000 cc. volume and an additional 4 pints of cell suspension was begun at 5:00 a. m. the following morning. The ninth pint was started as whole blood on entrance into the operating room. It was estimated that 1 or 2 pints (0.48 or 0.95 L.) might be lost during surgery, so 2 additional pints of whole blood was administered during this time. The patient experienced no shock and at 4:30 p. m., approximately 24 hours after admission, his red blood cell count was 4½ million.

There was no fear of overload reaction as might have been had 11 pints (5.2 L.) of whole blood been administered within a 24-hour period.

COMMENT

The advantages of red blood cell suspensions are briefly recapitulated. Larger doses of blood cells may be given in a single transfusion, resulting in a shortened period of hospitalization and decreased cost to the patient. Beds are thereby released to other needy patients, and convalescence, often prolonged because of anemia, can be more rapidly accomplished with large red blood cell transfusions.

Cardiac patients in particular, because of their intolerance to measures which increase effective blood volume, may have anemia corrected more satisfactorily with blood cell suspensions than with whole blood. In all patients, transfusion reactions of the allergic type, which account for approximately one-half of all reactions seen at the blood bank, are greatly reduced.

Overload reactions in cardiac and pediatric patients are exceedingly rare when red blood cell suspensions are used.

In the operation of the blood bank, two transfusions, one of red blood cell suspension and one of plasma, are obtained from a single collection of blood. This is most important since it provides blood components needed by patients. It would be extremely difficult, if not impossible, to procure sufficient donors for immediate transfusion if only whole blood were given on a one for one replacement basis.

SUMMARY

The immediate availability of blood in many blood banks throughout the country has led to the increased demand on these banks for blood. In order to meet this demand it is necessary that the two major components of whole blood be used specifically.

The indications for the proper use of red blood cell suspension have been outlined, and a method of calculating the dose of red blood cells required by a patient has been presented. The method of preparation of cell suspensions is described.

The advantages of more specific transfusion therapy to the patient and to the hospital have been discussed. The proper use of red cell suspensions and plasma when indicated will result in making more blood available for those who need it.

Plasma should not be wasted by administering it with cells as whole blood when only cells are needed. This economy permits stock-piling of more plasma for emergency or wartime needs.

310 Ingraham Bldg. (Dr. Smith).

V 14
1951

Cancer in Childhood.—The death rate from cancer varies considerably in the different age groups of childhood; that is, from the ages of one to four it is 40 per cent higher than in the five to nine group, and 80 per cent higher than in the nine to fourteen group. This variation is clearly explained by the types of cancer tending to occur in each group and would be even greater if the leukemias were excluded, since the incidence of leukemia is almost constant throughout childhood. Those tumors considered specific for childhood occur mainly in the first few years of life and begin sharply to decline in incidence in the second period. In the third period, when a greater number of the more adult types of tumors are noted, the childhood varieties of the neoplasms occur only very rarely. Characteristic of infancy are the embryonal, sarcomatous or mixed tumors, of which the best known are the Wilms' tumor of the kidney, the various teratomas, the adrenal and retinal neuroblastomas, and the embryonal rhabdomyosarcomas, most of which occur before the age of three years and some of which are congenital. The development of these embryonal tumors on the basis of dysontogenesis, often within the span of intrauterine life, clearly sets them apart from the ordinary cancers of adult life.—Sophie Spitz, M.D., Cutaneous Tumors of Childhood, *Journal of the American Medical Women's Association*, June, 1951.

NEW TECHNIQUE FOR LOCAL TREATMENT OF BURNS

Raymond M. Curtis, M.D., John H. Brewer, Ph.D.
and
Ira W. Rose Jr., M.D., Baltimore

In a previous publication in 1944, two of us (R. M. C. and J. H. B.)[1] first advocated the use of a partially hydrolized casein in the local treatment of burns and wounds, and, to date, approximately 500 patients have been treated with this preparation. Early investigations using human serum and plasma, bovine serum and plasma, and human and bovine placental serum led us to believe that the ideal type of local therapy for burns would consist of a readily available inexpensive protein which would closely resemble human plasma protein or its basic amino acids, to which the human body would show no signs of sensitivity and which would not be toxic to tissue cells. After an exhaustive study of the proteins available, the most satisfactory preparation was found to be one made from casein. It was found that casein could be prepared in combination with other materials to make a gel which on drying would form a film. Casein is a phosphoprotein, precipitated from milk by dilute acids, and is a readily obtainable and inexpensive by-product of milk. Sodium lactate, also obtained from milk, is added as a plasticizer to make the film pliable on drying. Sodium lauryl sulfate is added to lower the surface tension of the gel; it makes for easier application, and it acts as a bacteriostatic agent. These ingredients are mixed, dissolved and sterilized by autoclaving. In this process the casein is converted to sodium caseinate and undergoes some hydrolysis. The solution after sterilizing is approximately neutral. From a physical point of view the material is a gel of about the consistency of heavy molasses and may be easily spread with a wooden spatula. Although this material is an aqueous gel and will solidify on freezing, it will return to its original consistency on thawing and when hermetically sealed in containers has been kept for several years with no evidence of any chemical change.[1]

Early in our investigations in 1942, it became apparent that the gel would not dry rapidly on the weeping surfaces of superficial burns. To overcome this we clinically experimented with various transparent, commercially prepared coverings. The one which proved the most satisfactory was prepared from polyvinyl chloride. This film was found to have certain disadvantages which could not be overcome.

We were stimulated to improve this technique as a result of the need for a more practical local burn treatment than those which are currently popular. We felt that such a treatment was needed not only for the usual civilian burn casualties but particularly for use in the treatment of large numbers of burn casualties such as one might see in the case of atomic warfare. Pearse and Payne,[2] after studying the injuries in Japan following the use of the atom bomb, estimated that 60 to 85% of all patients requiring medical attention after an atomic bombing will be burned.

This led to the investigation of other methods able to produce a protein film, insoluble in the body fluids, which could be set soon after application to the injured part. Many of the heavy metal salts, alkaline earth metals, rennet, and other substances were found to have the ability to produce such a film. The one most satisfactory from the clinical point of view was found to be zinc acetate.[3] This material was first applied as a solution over the protein gel on the skin. Later it was found that when gauze [1] impregnated with the metallic salt was placed over the protein gel the salt combined with the gel to produce a film within the meshes. Within minutes, depending on the concentration of the impregnated metallic salt, the gel rose into the gauze and formed a semipermeable membrane which prevented the local loss of serum protein from the burn but which did allow water slowly to evaporate from the wound.

Fig. 1.—Method of application of gel and gauze. The breast area shows gel in place prior to application of the gauze. The chest area shows both gauze and gel in place.

The most satisfactory gauze has been found to be a 6-ply, loosely knit gauze containing approximately 30 mg. of zinc acetate per square inch of gauze. The chemically treated gauze can be sterilized without interfering with its ability to coagulate the gel. This can be done by autoclaving.

METHOD OF TREATMENT

With an aseptic technique any loose necrotic skin is removed. No cleaning of the burn is attempted unless grease has previously been applied, in which case this is removed with ether. The partially hydrolyzed casein gel is applied to the superficial as well as the more deeply burned areas with a sterile wooden spatula and a mop-

Read before the Section on Surgery, General and Abdominal, at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

From the Department of Surgery, Union Memorial Hospital (Dr. Curtis and Dr. Rose), and the Biological Research Laboratories of Hynson, Westcott & Dunning, Inc. (Dr. Brewer).

1. This material is "Zinax" Gel and "Zinax" Gauze, manufactured by Hynson, Westcott & Dunning, Inc.

2. Pearse, H. E., and Payne, J. T.: Medical Progress: Mechanical and Thermal Injury from the Atomic Bomb, New England J. Med. **241**: 647-653 (Oct. 27) 1949.

3. This was suggested by Mr. A. E. Stickles, Chemical Research Laboratory, Hynson, Westcott, & Dunning, Inc.

ping motion to at least 1/16 in. (0.17 cm.) in thickness. This is much thicker than the usual application of ointments to the skin. The whole is covered with strips of the impregnated gauze and then wrapped with a bandage (Fig. 1). An elastic bandage has been found to offer certain advantages such as conformity to the part, but care is taken not to pull the bandage tightly.

It is essential that there is an adequate layer of gel between the burn and the gauze. As an alternative method of application a heavy coating of gel about ⅛ in. (0.32 cm.) thick may be spread on the gauze and then applied to the burn. This method is preferable in sites such as the posterior surfaces of the extremities. It is also advantageous in that it eliminates the possibility of incompletely covering the burn.

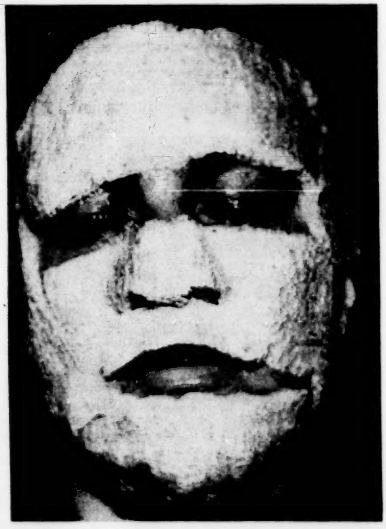


Fig. 2.—On the face, and on small burns, the gel and the gauze may be applied as a patch which serves as the only dressing.

When the extremities are dressed, the impregnated gauze is laid longitudinally over the extremity, not encircling the part, in order to prevent any abnormal pressure points.

On the face, and on small burns, the gel and the gauze may be applied as a patch which serves as the only dressing (Fig. 2).

The dressing can remain in place as long as is desired; however, when there is only erythema or a first-degree burn it is usually removed the following day. In the case of superficial second-degree burns, it is left intact for approximately 14 days or until it separates from the burned surface. In the deep second-degree and third-degree burns that may necessitate grafting we have found that the surface is frequently ready for grafting within six to 10 days and have found it advantageous to re-dress the burn once or twice during this period in order to hasten the cleanup of the dead tissue.

If the dressing remains on the wound in the superficial second-degree burns until healing has occurred, it usually comes away from the wound readily. If, however, one desires to remove the dressing at an earlier time, this can be more easily done by soaking the dressing with warm isotonic sodium chloride solution. In the deep second-degree and third-degree areas, as the dead skin is lysed the film separates from the surface of the wound.

RESULTS OF TREATMENT

To date, 561 [4] burns have been treated in the manner described. One hundred and fifteen of these represent our personal cases, and the therapy discussed in this paper was applied to them. One case is illustrated and described in detail.

REPORT OF CASE

C. S., a white male aged 13, was admitted to Union Memorial Hospital on Dec. 17, 1950, one-half hour after having accidentally burned his right leg when paint remover had become ignited and had set his trousers on fire.

Fig. 3.—Initial burn after complete dressing.

On his admission to the accident room, examination revealed superficial and deep burns of the right leg from the knee to the ankle.

The partially hydrolyzed casein gel and the zinc acetate-impregnated gauze were applied as in our description of the method of treatment (Fig. 3).

On Dec. 23, six days after admission, this patient's leg was dressed, and it was noted that the superficial burns were well healed, and the dead skin which had been present in the deeply burned sites was completely lysed. Areas of fat and corium were plainly visible (Fig. 4).

The same type of dressing was reapplied, and on Dec. 26, nine days after admission, this dressing was removed, and, without any débridement, two dermatome skin grafts 0.0014 in. (0.0036 cm.) in thickness were applied to the subcutaneous fat in that portion of the burned leg where the dead skin had been completely lysed (Fig. 5).

On Dec. 30, the dressings were removed and revealed a 100% take of the skin grafts.

The patient was discharged from the hospital on Jan. 14, 1951, 29 days after admission. He returned for an office visit on March 15, 1951, at which time there was evidence of very little superficial scarring (Fig. 6).

This case clearly points out the rapidity with which one can proceed with grafting in the cases where the burn is a deep second-degree or third-degree burn.

The results obtained with this treatment of burns among ambulatory as well as hospitalized patients have been most gratifying. There has been a relief of pain

4. This total represents 412 ambulatory industrial burns, which are to be reported in another publication by Dr. Walter E. Fleischer, Baltimore, and 22 burns serious enough to warrant hospitalization, which are to be reported in another publication by Capt. Paul E. Spangler, Portsmouth Naval Hospital.

that can be accounted for only in part by the exclusion of air and the mechanical immobilization which the dressing provides.

The importance of this type of immobilization for the prevention of the local protein loss by the damaged capillaries and the extra-cellular accumulation of a fluid

Fig. 4.—The semipermeable membrane is shown partially removed six days after admission. There is lysis of third degree areas with subcutaneous fat and corium visible.

high in protein with its subsequent interference in the local cellular metabolism of the injured cells, with its subsequent clotting and fibrosis, was demonstrated in 1943 by Glenn, Gilbert and Drinker.[5] These authors were able to minimize this increase in capillary permeability by the experimental utilization of plaster casts on burned extremities.

The protein film tends to adhere to the injured surface, thus providing a type of immobilization and tissue support which cannot be accomplished by the usual pressure dressing. Clinically and experimentally, we have found that this type of dressing diminishes the superficial loss of fluid as well as the loss of protein into the burned area. We have been repeatedly impressed in our clinical cases with the ability of this dressing to prevent blistering in the superficial burns and edema of the injured parts in the extensive ones.

Fig. 5.—Application of dermatome skin grafts nine days after admission.

In the first-degree and superficial second-degree burns, the protein film is readily removed from the burn surface when desired. In the deep second-degree and third-degree burns the dead skin appears to be digested by the individual's own enzymatic and phagocytic systems and the film is separated in this process. This occurs with such rapidity that third degree burns have been grafted as early as the ninth day, as shown by the case illustrated.

Although the casein gel in contact with the impregnated gauze is changed to an insoluble state, the gel in direct contact with the wound is not immediately coagulated but may remain in its gel state for a short time. Thus, by application of a partially hydrolyzed casein solution, we may be providing the best possible medium in which these injured cells of uncertain status can grow and develop.

In addition to the local treatment herein described we are fully cognizant of the need, particularly in the severe burns, for adequate systemic treatment—antibiotics, plasma, blood, high-protein intake, hormonal and vitamin therapy—and we use these in our serious burns.

SUMMARY

1. A new method for the treatment of burns and wounds is suggested. It is comprised of a partially hydrolyzed casein gel which is applied to the burned area and is then covered with gauze impregnated with zinc acetate. The gel is set, forming a semipermeable membrane which prevents the superficial protein loss, and, by the support

Fig. 6.—End result two months after patient's discharge from the hospital.

given the damaged capillary bed, diminishes the protein loss into the burned area, thus minimizing local cellular damage and shock.

2. There is relief of pain, a minimum of infection, and a splinting of the injured part.

3. This method of treatment permits early grafting by allowing the body's own enzymatic and phagocytic systems to débride the area of deep burn.

4. The described method is simple and easy to apply and can be used by untrained personnel.

2919 St. Paul St.

5. Glenn, W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed-Plaster Method, with Certain Physiological Considerations Implicit in the Success of this Technique, J. Clin. Invest. 22: 609-625 (July) 1943.

Silent Prostatism.—The absence of prostatic enlargement rectally cannot be dismissed as lack of evidence of obstruction of the bladder neck. The small, firm prostate may have become so infected over the years that the hyperplasia has undergone complete fibrosis, producing a cartilaginous-like ring almost completely obliterating the bladder neck. Also, inflammation of the prostate in youth may have produced the condition variously known as contracture, sclerosis or fibrosis of the bladder neck. A patient with such an obstruction usually seeks relief earlier in life than the patient with a hyperplastic prostate. Conservative measures such as dilatation, however, may prolong this condition beyond middle age. Intravesical protrusion of the prostate may reveal only minimal rectal findings, yet the middle lobe may be large, and effectively prevent emptying of the bladder. —Earl E. Ewert, M.D. and Howard J. Summons, M.D., "Silent" Prostatism, *The Surgical Clinics of North America*, June, 1951.

OCCURRENCE OF SKIN PIGMENTATION DURING MESANTOIN® THERAPY

Harriot Hunter, M.D.
and
Dalton Jenkins, M.D., Denver

Since the introduction of mesantoin® (3-methyl-5,5-phenylethylhydantoin) as an anticonvulsant in 1945,[1] there have been many reports of various toxic manifestations. However, we have found no mention of the reaction described in this paper. It is our purpose to report six cases of idiopathic epilepsy, which were partially controlled by large doses of mesantoin® and other anticonvulsants, in all of which a peculiar identical pigmentation of the skin appeared on the face and neck in the course of therapy. No conclusive evidence has been obtained to indicate that this represents a toxic reaction, but there is strong presumptive evidence to that effect.

REPORT OF CASES

CASE 1.—I. B. S., a 33 year old white housewife, was first seen in the clinic on March 8, 1948. She complained of "fainting spells" since 1941. These spells were subsequently described so as to leave no doubt that they were grand mal convulsions. They had occurred irregularly and infrequently over a period of years, but during pregnancy increased in frequency to about once a month. The baby was born on Jan. 22, 1948, and since that time, seizures had been even more frequent. The first electroencephalogram tracing was normal, but a sleep tracing done a month later was classified as "abnormal paroxysmal S-2" (very slow). All other examinations, including roentgenograms of the skull and neurological tests were normal, and a diagnosis of idiopathic epilepsy was made. Hypoglycemic attacks on the basis of hyperinsulinism were considered but never substantiated; fasting blood sugar was normal, but two glucose tolerance curves were abnormally flat. The only other finding worthy of note was a low blood pressure: 110 systolic and 68-78 diastolic.

Mesantoin® therapy, ½ tablet (50 mg.) a day, was instituted and was gradually worked up to a maintenance dose of 100 mg. three to four times a day. No sensitivity was noted. Blood count remained within normal limits. (The only other medication during the first year was amphetamine [benzedrine®] sulfate, 2.5 mg. three times a day for sleepiness. This was discontinued after seven months on account of unexplained weight loss.) Seizures immediately decreased in frequency and during the first year of therapy numbered only seven; the last one, which occurred on March 1, 1949, was related directly to the discontinuance of medication for a repeat electroencephalogram. From that date until the present time, the patient has had only one mild spell on June 17, 1949.

On April 10, 1950, on a routine visit, the patient had a patchy, brownish pigmentation over the face (fig. 1). She was complaining of fatigue, continued failure to gain weight, and an undue craving for sweets. A tentative diagnosis of adrenal cortical hypofunction was made; the patient was reexamined in medical clinic and admitted to the ward for a Robinson-Kepler-Power water test. At this time, the following results were obtained from examinations: Blood pressure was 100 systolic and 60 diastolic. There were 4,600,000 red blood cells with hemoglobin of 13.1 Gm.; white blood cells numbered 6,000 with 43% neutrophilic filamented leukocytes, 15% neutrophilic nonfilamented leukocytes, 39% lymphocytes, and 3% monocytes. Urine showed a 1 + albumin. Roentgenograms of the abdomen and chest were normal. Basal metabolic rate was + 3. Glucose tolerance curve showed a fasting blood sugar of 89 mg. per 100 cc., and 96, 86, and 90 mg. per 100 cc. at the end of one, two, and three hours, respectively. In procedure 2 of the Robinson-Kepler-Power water test, the value for "A" was 12. Thorne's eosinophil test was not done at this time. Serum amylase was 48 units per 100 cc. Dermatological consultation described the pigmentation as simulating "chloasma" or the "mask of pregnancy" and mentioned adrenal cortical hypofunction as one possibility. Pregnancy was subsequently ruled out. No diagnosis was made, and no treatment was instituted at this time. In June the patient was feeling much better and noted that she had had no seizures for a full year. She then began spontaneously to cut down on her dose of mesantoin® until by the end of July she was taking only "an occasional dose." At a visit on July 31, the pigmentation was remarkably cleared. She was advised to discontinue mesantoin® altogether. A repeat electroencephalogram on July 22 was reported as within normal limits and "considerably improved over past tests." On August 1, she was admitted for a repeat Robinson-Kepler-Power water test, in which the value of "A" was 31. Blood count at this time was within normal limits. At the present time, the patient is still free from seizures, is taking no mesantoin,® and has no abnormal pigmentation (fig. 2). No other evidence of adrenal cortical hypofunction was found, and the first Robinson-Kepler-Power water test was, therefore, considered to be a false-positive.

CASE 2.—L. M., a 29 year old single white woman, had been seen in the Colorado Epilepsy Service since 1944. She had had seizures since the age of 5 years. Grand mal attacks, which were occurring about once a month, were fairly well controlled by diphenylhydantoin (dilantin®) sodium, 100 mg. four times a day. In July, 1947, she was placed on trimethadione (tridione®), 32 mg. once a day because of reported "dizzy" or "light-headed" spells. Blood counts during that period were reported normal. In January, 1948, she had two grand mal seizures, and medication was changed abruptly to hydantal® (combination of mesantoin® and phenobarbital sodium), one tablet three times a day. Diphenylhydantoin sodium in oil, 100 mg., was administered at bedtime, and trimethadione was continued until August, 1948. Blood counts continued normal. At the time hydantal® was begun, an upper respiratory infection was noted, and the patient was examined in ear-nose-throat clinic; penicillin and sulfa drugs were administered. In retrospect, this possibly represented a mild toxicity, but it was not thought so at the time. A note on June 21, 1948 states: "Patient complains of yellow skin, not objectively demonstrable at this time." Trimethadione was stopped in August, 1948, and mephobarbital (mebaral®) was begun. The patient was then maintained on mesantoin,® 100 mg. three times a day, and mephobarbital, 100 mg. twice a day. No seizures were reported. In November, 1948, it was reported that the patient had "an acneiform eruption, somewhat more erythematous and pustular than acne, distributed over the left lower face, left arm, left deltoid region." She had also spent a week in bed for "sinus trouble." Throat and tongue were essentially clear. The attending physician at that time said: "I do not believe the papulo-pustular eruption is due to mesantoin or mebaral; probably staphylococcic and topical because of distribution." Sulfathiazole ointment was recommended. A note on Feb. 12, 1949, states: "Papulo-postular eruption almost cleared; evidently unrelated to mesantoin."

Medication was continued; mesantoin® was increased to four times a day in February, 1949, and spells were controlled in spite of much family trouble. Several examinations in ear-nose-throat clinic were essentially normal but indicated that the patient was subject to frequent upper respiratory infections even before mesantoin® was instituted. In June, 1949, the patient re-

Instructor in Medicine (Dr. Jenkins).
Associate Professor of Psychiatry (Dr. Hunter).
From the Department of Psychosomatic Medicine, University of Colorado Medical Center.

1. Loscalzo, A. E.: Treatment of Epileptic Patients with a Combination of 3-Methyl 5,5-Phenylethyl-Hydantoin and Phenobarbital: Preliminary Report, J. Nerv. & Ment. Dis. **101**: 537 (June) 1945.

V 14
1951

ported by letter an "ulceration of the mouth." Examination on July 18, 1949, revealed "aphthous ulcers in stoma with mesantoin dosage of four tablets a day. . . . Papulo-aphthous ulcer over buccal surface opposite molars of either side." Hydrogen peroxide was recommended. Blood studies continued to be normal until the last one done on April 17, 1950, showing 6,000 white blood cells with 7% neutrophilic nonfilamented leukocytes, 52% neutrophilic filamented leukocytes, 28% lymphocytes, 10% monocytes, 3% eosinophils, and an "occasional atypical lymphocyte." Patient was continued on mesantoin* four times a day; stomatitis cleared up, but occasional "boils" appeared here and there. Patient had many varied complaints and was sent to urology clinic. Normal intravenous pyelograms were reported, but urine showed albumin, pus cells, and red cells. Catheterized specimen later was normal. There was inguinal lymphadenopathy. She was sent to medical clinic on Feb. 6, 1950, because of persistent upper respiratory infection, sinusitis, cough, frequency, and urgency of micturition. No skin changes were noted at this time. Glucose tolerance test showed a normal curve. Blood pressure was 100 systolic and 70 diastolic. Nonprotein nitrogen was normal.

Fig. 1 (case 1).—Photograph showing patchy, brownish pigmentation over the face during mesantoin* therapy.

On April 17, 1950, notation states "gradually increasing fawn-colored pigmentation, especially of forehead and lower face." This pigmentation was noted to be identical with that described above in case 1. The patient was admitted to the ward for metabolic studies on July 7, 1950. At the time of admission, she had "bronze pigmentation of the face," with patchy distribution, and an "erythematous rash covering the neck" (fig. 3). Except for congenital cataracts, examination was otherwise essentially normal. Blood pressure was 120 systolic and 80 diastolic. During hospitalization, the patient ran a low grade fever; chronic otitis media was discovered and treatment instituted. Blood count showed 4,500,000 red blood cells and 10.8 Gm. hemoglobin; white blood count was 6,800 with 72% polymorphonuclear forms, 23% lymphocytes, 4% monocytes, and 1% eosinophils. Thorne's eosinophil test gave a result of 69% decrease. Robinson-Kepler-Power water test gave a normal reading. After complete studies, the possibility of decreased adrenal gland function was ruled out. Diagnosis was idiopathic epilepsy and toxic pigmentation of the face. At the present time, blood studies are normal. The patient continues on mesantoin,* 100 mg. four times a day, and mephobarbital, 50 mg. two times a day, with no seizures.

Case 3.—M. B., a 23 year old single white woman, was first seen in clinic on March 23, 1949, giving a history of an infection at age 11 months, with subsequent episodes of unconsciousness and convulsions. After complete work-up in medical, neurological, and epilepsy clinics, a diagnosis of "post-encephalitic

Fig. 2 (case 1).—Photograph showing disappearance of abnormal pigmentation after mesantoin* therapy was discontinued.

brain disease with convulsive disorder" was made. Electroencephalogram was conclusive, with pathology predominantly in the frontal lobes. Spinal fluid examination was normal, except for low protein (10 mg. per 100 cc.). Blood studies were normal. Blood pressure was 96 systolic and 80 diastolic. Glucose tolerance curve was as follows: fasting blood sugar of 95 mg. per 100 cc.; at the end of one, two, three, four, five, and six hours, the readings were 94, 78, 80, 64, 62, and 66 mg. per 100 cc., respectively. Skull roentgenograms were normal. Patient was

Fig. 3 (case 2).—Photograph showing bronze pigmentation of the face with patchy distribution.

started on diphenylhydantoin sodium every day and phenobarbital sodium twice a day. On May 23, diphenylhydantoin sodium was increased to 100 mg. twice a day. This was continued until Aug. 22, 1949 when gingival hypertrophy and continued seizures led the physician to change the medication to mesantoin* until a maintenance dose three times a day was established; phenobarbital sodium was continued. Seizures continued until early 1950, but have been absent for five months.

On May 29, 1950, on a routine visit, a brownish patchy pigmentation was noted over the face, neck, and arms on mostly exposed areas, said to have been present for several months and to have "blossomed out" after exposure to the sun (fig. 4). The patient was admitted to the hospital for metabolic studies on June 26, 1950. There were 4,080,000 red blood cells with hemoglobin of 12.35 Gm.; white blood cells numbered 4,400 with 48% neutrophilic filamented leukocytes, 40% lymphocytes, 9% monocytes, and 3% eosinophils. The result of the Robinson-Kepler-Power water test was normal with 38 as the value of "A." The patient gave a normal response to Thorne's eosinophil test. No evidence of adrenal cortical hypofunction or adrenal insufficiency was found. Biopsy of the skin in this case (the only biopsy performed, since the pigment was on the arms as well as on the face) showed "a moderate but not excessive amount of yellow-brown melanin pigment granules in the basal layer of the epidermis." A pathologic diagnosis of "dermatitis, chronic, mild" was made. The only other abnormal finding during hospitalization was a bilateral cholesteatoma, which had been present for years.

The patient continues to have no seizures and is being maintained on hydantal,* five times a day, and phenobarbital sodium ¾ grain (50 mg.) at bedtime.

CASE 4.—P. C., a 35 year old single white schizoid woman, was first seen on Aug. 23, 1948, complaining of grand mal seizures since the age of 15. After complete work-up, a diagnosis of idiopathic epilepsy was made, substantiated by electroencephalographic findings, and the patient was placed on diphenylhydantoin sodium, 100 mg. three times a day, and phenobarbital sodium, 30 mg. three times a day, on Aug. 30, 1948. In spite of an increase of diphenylhydantoin sodium to four times a day, the patient continued to have seizures, and on Feb. 21, 1949, mesantoin* was instituted slowly. On March 21, 1949, after one month of therapy, the patient complained of increasing seizures and dissatisfaction with therapy and was again given diphenylhydantoin sodium medication. Mesantoin* was discontinued. The patient continued to have seizures, as many as 10 to 15 a month, and again mesantoin* therapy was begun on Nov. 28, 1949. No intolerance or sensitivity had been noted. Blood counts were normal.

Fig. 4 (case 3).—Photograph showing brownish, patchy pigmentation over face and neck.

The patient continued to receive diphenylhydantoin sodium, 100 mg. four times a day, and phenobarbital sodium, 65 mg. four times a day, as well as mesantoin,* 100 mg. three times a day. The attacks changed somewhat in character and decreased somewhat in frequency, but the patient continued to complain. On May 29, 1950, the patient was instructed to discontinue the mesantoin,* but this was not done. On July 24, 1950 the patient was still taking mesantoin,* three times a day, and at this time, the same brownish, discolored patchy pigmentation as described in the other cases was noted (fig. 5). Because of the limited intelligence of the patient and her mother, it was impossible to tell when this darkening of the skin first appeared.

Fig. 5 (case 4).—Photograph showing same brownish, patchy pigmentation as noted in other cases.

This patient has not been studied for adrenal insufficiency, but there is no clinical evidence of such a condition at this time. She has not been taking mesantoin* for several weeks, but the skin has not cleared.

CASE 5.—D. H., a 29 year old man, has been seen in clinic since Aug. 23, 1948. Previous to that, he had visited the outpatient department of the Psychopathic Hospital since 1934. At that time he gave a history of having had convulsive seizures since 1 year of age. Final diagnosis was idiopathic epilepsy in a dull normal individual. During the years he has attended the clinics, he has kept a careful report of all seizures and in spite of anticonvulsant therapy, has an average of 10-15 seizures a month, sometimes as many as 14 to 15 in one day, with the longest free period being about three weeks. On Jan. 17, 1949, he was started on mesantoin,* 50 mg. daily for one week, and worked up to a dose of 100 mg. three times a day at the end of a month. Maintenance dosage of anticonvulsant medication was finally established as diphenylhydantoin sodium, 100 mg. four times a day, phenobarbital sodium 100 mg. four times a day, and mesantoin,* 100 mg. four times a day. The patient was then maintained on this dosage until the present time without evidence of any sensitivity or toxicity. He is dull

mentally, lives in a protective environment, and does not wish to change his completely dependent status, and, therefore, he did not object to such large amounts of medication. It did not seem to affect his mental status except to produce drowsiness. His seizures have decreased in frequency until at the present time he has not had a spell in over four months.

Pigmentation on the face previously described above was not noticed until a visit to the clinic on July 3, 1950 (fig. 6). The patient was utterly indifferent about it and stated that he had not noticed it but that it had "probably been there for a long time." When later questioned about it, the family agreed that it had appeared more prominent during the past year, but they had not paid much attention to it. Since there was doubt about the onset of the pigmentation in relation to the administration of mesantoin,* at first it was thought best not to include the patient in our series. However, later an opportunity presented itself to hospitalize him for study. His mother called and complained that the patient was having a shaking chill and high fever (although she was unable to take his temperature) and that he slept unduly for as long as 48 hours at a time. The patient was hospitalized.

On admission, physical examination was unremarkable except for the pigmentation on the face and neck and previously noted mental dullness. Blood studies were normal. Eosinophil response was within normal limits. Temperature during hospitalization was normal. No evidence of toxicity was noted. Although the patient appeared somewhat stupid to the attending physician, it should be noted that his mental status has not changed appreciably over the years of his contact with us.

CASE 6.—B. B. Z., a 35 year old married woman, has not been studied as thoroughly as the other cases, because she resides some distance from the hospital. She is a close relative of the patient in case 1. In the clinic where she first appeared in

Fig. 6 (case 5).—Photograph showing pigmentation over the face.

May, 1948, a diagnosis of idiopathic epilepsy was made, and a maintenance dose of mesantoin,* 100 mg. four times a day, and diphenylhydantoin sodium, 100 mg. four times a day, was established, with an "occasional" dose of phenobarbital sodium, 65 mg. Her seizures have been fairly well controlled on this medication; according to the patient, she has had no seizures at all in over one year.

Pigmentation of the face was first noticed by this patient after her cousin had informed her of her own experience in the spring of 1950 (fig. 7). No other evidence of toxicity or sensitivity was noted. Blood studies were normal. The patient was not hospitalized.

COMMENT

Cutaneous rashes of various types have been reported frequently as manifestations of mesantoin* toxicity,[2] but, so far, simple pigmentation of the skin has not been suggested. Since the development of the pigmentation is insidious and almost unnoticeable and apparently is not associated with any remarkable signs of severer toxicity, it has escaped notice until very recently when several cases came almost simultaneously to our attention. It is likely that other instances of similar pigmentation may have escaped the attention of other clinical observers and that this report may aid in the detection and investigation of other cases. Since this pigmentation may represent the forerunner of severer toxic signs, such cases would bear careful observation.

Fig. 7 (case 6).—Photograph showing pigmentation of the face.

2. Aird, R. B.: The Treatment of Epilepsy with Methylphenylethyl Hydantoin (Mesantoin), California Med. **68**: 141 (March) 1948. Arieff, A. J.: Mesantoin in Severe Epilepsy, Quart. Bull. Northwestern Univ. M. School **22**: 349 (April) 1948. Belinson, L.: Incidence of Sensitivity to Mesantoin: Effect of Dosage, Dis. Nerv. System **9**: 252 (Aug.) 1948. David, N. A.: Methyl Hydantoin (Mesantoin) in the Treatment of Epilepsy, J. Nerv. & Ment. Dis. **108**: 118 (Aug.) 1948. Fetterman, J. L., and Victoroff, V. M.: Mesantoin in Epilepsy: A 3 Year Study, Dis. Nerv. System **10**: 355 (Dec.) 1949. Garvin, J. S., and Gibbs, F.: Mesantoin Toxicity, Dis. Nerv. System **11**: 48 (Feb.) 1950. Loscalzo, A.: The Control of Epilepsy, J. A. M. A. **135**: 496 (Oct. 25) 1947. Ruskin, D. B.: Mesantoin (Methylphenylethyl Hydantoin) in Treatment of Epilepsy in a State Hospital, Arch. Neurol. & Psychiat. **60**: 484 (Nov.) 1948. Bloom, N.; Lynch, J. P., and Brick, H.: "Mesantoin" Poisoning with Aplastic Anemia and Recovery, J. A. M. A. **138**: 498 (Oct. 16) 1948. Kozol, H. L.: Mesantoin in Treatment of Epilepsy, Arch. Neurol. & Psychiat. **63**: 235 (Feb.) 1950. Davies, R. R.; Fisch, C., and Tischer, E. P.: Pancytopenia Due to Mesantoin, New England J. Med. **242**: 863 (June 1) 1950. Weller, R. W., and Metcalfe, J.: Fatal Pancytopenia Following the Use of "Mesantoin," New England J. Med. **241**: 17 (July 7) 1949.

To date, we have been unable to demonstrate any other signs of toxicity in any of these patients. In three cases there have been complaints of severe headache, which had not been a prominent complaint before. One person, the only man in the series, has been drowsy and lethargic, but he is also taking large amounts of two other anticonvulsants. Also, in this case, a reportedly sudden rise in temperature accompanied by chilling subsided rapidly; by the time of hospitalization the following morning, there was no fever. In three other cases, there was a mild, transitory elevation of the temperature during the hospital course; in one of these, the fever was unexplained, but in the other two, it was associated with a chronic middle ear infection, which was discovered during physical examination. No indication of any other intercurrent disease has been noted in any of the cases.

Several features are common to most of these cases. All but one of the patients are women. All but one have severe idiopathic epilepsy with distinctly disturbed electroencephalograms and seizures that have been brought under control only recently by the use of large doses of mesantoin.* All six patients had been taking mesantoin* for a year or more when the pigmentation was first noted. All but one have had other anticonvulsants besides mesantoin,* but no other drug is common to all six cases, and no case of pigmentation has occurred in any patient who is not currently taking mesantoin.* Most of the patients are mentally dull and have some evidence of organic involvement. All have somewhat low blood pressures.

As to the nature of the pigmentation, there has been considerable speculation and disagreement among observers. At first observation, the dermatologist thought that in at least two of the cases, it was "chloasma, possibly associated with pregnancy." Pregnancy was definitely ruled out in all five women. Adrenal cortical hypofunction was also mentioned as being responsible and was strongly considered in the first three cases. All these three had several remarkable features in common: they were young women who had all complained of fatigue, loss of weight, and lack of energy and had low blood pressures and abnormally flat glucose tolerance curves. We decided to investigate the status of the adrenal glands in these cases in order to determine whether the skin pigmentation bore any relation to impaired adrenal function.

Therefore, four of the six cases were admitted to the hospital with the tentative diagnosis of adrenal cortical hypofunction and were studied for adrenal insufficiency. On the basis of negative results obtained in each case in all tests administered, we concluded that there was no impairment of adrenal function. Complete blood studies were within normal limits in all six cases. Urine studies gave no evidence of any homogentisic acid or porphyrins.

Skin biopsy showed the pigment to be melanin. It has been suggested that the mesantoin* plays a role similar to that of the sulfa drugs in making the skin sensitive to the sun's rays. However, in only one case has there been any prolonged or undue exposure to the sun. In a further investigation along these lines, we will attempt to verify this by having the patient deliberately expose the arms and legs to the sun and performing a biopsy of the area if pigmentation develops.

In the first case, the epilepsy was considerably milder than in any of the other five cases. After a year in which the patient had been free of seizures, she decided to cut down on the dose of mesantoin.* After the use of minimal doses for several weeks, the skin pigmentation began to be much less evident. For the past three months, she has been taking no drug and remains free of seizures, and her skin is almost entirely clear. Further investigation is being contemplated with the full cooperation of the patient in order to determine whether or not the mesantoin* is directly responsible for the pigmentation of the skin. The patient will be given mesantoin* again in doses of 100 mg. four times a day and observed for the reappearance of the pigment. Already, with the disappearance of the pigmentation immediately after cessation of mesantoin,* this case gives prima facie evidence for the theory that the drug has played some role in its causation.

At the present time, all six cases are being watched for the development of any further signs of toxicity. Since control of the seizures has been especially difficult in five of these cases until the use of mesantoin,* and since there has been no real evidence of any serious toxic effects, the drug has not been reduced or discontinued in four of the cases.

SUMMARY

Six cases of idiopathic epilepsy during mesantoin* therapy are presented. A cutaneous pigmentation that appeared during therapy is described. Four of the patients were hospitalized, but clinical studies failed to reveal any basic functional disturbance of the adrenal glands. The question is raised as to the role of mesantoin* in the production of this pigmentation, and further investigation along these lines is being made.

University of Colorado Medical Center, 4200 E. Ninth Ave. (Dr. Hunter).

Medical Writing.—True, scientific articles must present the whole truth; to suppress inconvenient evidence is fraud. But if there is a great deal of inconvenient evidence, it is probably because the time has not yet come to present anything. More work and thought are required. But when observations can be regularly repeated and the worker is clear about his interpretation, it is not necessary for him to unload every figure from his records into the article written for publication. The false scents, the contradictory observations, the tentative experiments which precede the fruitful work can be briefly and honestly presented in a single paragraph if they are relevant. They should be omitted if they prove irrelevant, as they often do.

Every repetition, even of a successful experiment, need not be presented in detail. The results of a series of confirmatory observations can often be quoted as means with statistical treatment of the data; and a few illustrative experiments or case-summaries may suffice to show the kind of detail from which the work as a whole has been made. Properly understood and honestly practiced, therefore, selection is as important and valuable in scientific literature as in imaginative writing.—J. W. Howie, M.D., On Writing to Be Read, *Lancet*, Aug. 25, 1951.

V 147
1951

CLINICAL NOTES

SYSTEMIC BLASTOMYCOSIS COMPLICATED WITH PREGNANCY

REPORT OF A CASE, WITH CLINICAL COURSE AND IMMUNOLOGIC REACTIONS

Ray O. Noojin, M.D.
and
Hugh B. Praytor, M.D., Birmingham, Ala.

It is known that systemic blastomycosis is usually a fatal disease.[1] Smith has pointed out that the prognosis depends partly on the extent of infection and partly on the immunologic response of the patient.[2] Uterine involvement in systemic blastomycotic infection has been reported.[3] This report concerns a pregnant woman with proved cutaneous and pulmonary infection with Blastomyces dermatitidis. Signs and symptoms of systemic blastomycosis developed in the patient during her second trimester. The detailed clinical, therapeutic, and immunologic developments are presented. Immunologic studies were also carried out on the infant on three occasions during the 12 mo. following birth.

Fig. 1.—Facial eruption showing nodular, verrucous lesions in a patient with systemic blastomycosis.

REPORT OF CASE

O. P. C., a 21-yr.-old Negro woman, pregnant for six months, was admitted to the hospital on May 9, 1949, complaining of a cough and an eruption on her face. One week prior to admission an enlarging lesion appeared on the left eyelid. Similar lesions developed on the right eyelid, forehead, chin, upper extremities, and back. A cough, occasionally productive of small quantities of sputum streaked with bright red blood, had persisted for one and one-half months. During the same period weakness and fever were noted. Pelvic pain and minimal vaginal bleeding developed during the first few days of illness. In spite of bed rest and administration of penicillin and one of the sulfonamides, the patient's cough had persisted. Sharp pain occurred along the left costal margin during attacks of coughing. Increased night sweats had been present for one week.

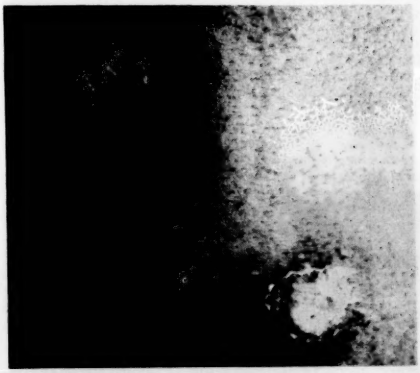


Fig. 2.—Nodulo-ulcerative, verrucous lesions on the back of a patient with systemic blastomycosis.

Physical examination revealed a temperature of 98.8 F., a respiratory rate of 32, and a pulse rate of 86. The patient was a well-nourished young Negress who did not appear ill except for the presence of several nodular crusted cutaneous lesions. These lesions were approximately 1 cm. to 1.5 cm. in diameter and involved the eyelids, nose, forehead, scalp, and chin (Fig. 1). Two ulcerated lesions were present on the upper back (Fig. 2). There were several firm nodules over the arms and legs. Slight injection of the right conjunctiva was noted. Several nontender lymph nodes were palpable in both anterior cervical areas. Respiratory excursion was diminished on the right side. Posteriorly at the right lung base below the angle of the scapula, decreased fremitus, dulness, and distant breath sounds were noted. No rales were heard. Anteriorly the right lung appeared to be clear except for slightly increased resonance. The left lung was clear. The heart was normal. The blood pressure was 108/60. The abdomen was distended. The uterine fundus was extended to the umbilicus. A small nodule was present in the pubic area. No other abnormal physical findings were noted.

Laboratory examination revealed a red blood cell count of 3,050,000. The hemoglobin determination was 10 gm. (by the Haden-Hausser method). The color index was 1.06. The white blood cell count was 10,900, and the differential formula disclosed 9 lymphocytes, 2 monocytes, 81 polymorphonuclear neutrophils, and 6 stab forms. The urinalysis, a blood bromide test, and a Kahn serologic test for syphilis were negative. A biopsy of one of the cutaneous nodules revealed numerous budding,

From the Department of Dermatology and Syphilology, Medical College of Alabama.

The laboratories of the Division of Mycology, Duke University, and the Communicable Disease Center of the Public Health Service, Chamblee, Ga., performed the complement-fixation tests reported.

1. Jones, R. R., Jr., and Martin, D. S.: Blastomycosis of Bone: A Review of 63 Collected Cases, of Which 6 Recovered, Surgery **10**: 931-938 (Dec.) 1941.

2. Smith, D. T.: Immunologic Types of Blastomycosis: A Report on 40 Cases, Ann. Int. Med. **31**: 463-469 (Sept.) 1949.

3. Hamblen, E. C.; Baker, R. D., and Martin, D. S.: Blastomycosis of the Female Reproductive Tract, with Report of Case, Am. J. Obst. & Gynec. **30**: 345-356 (Sept.) 1935.

double-contoured, oval bodies diagnostic for B. dermatitidis (Fig. 3). Similar budding organisms could be demonstrated in pus taken from the cutaneous lesions. Sputum examination revealed no acid-fast bacilli but did reveal B. dermatitidis. No fungi could be demonstrated in the spinal fluid. The total serum proteins were 6.4 gm. per 100 cc., which included albumin 2.7 gm., and globulin 3.7 gm., per 100 cc. The A-G ratio was 0.71. An intracutaneous test with 1: 10,000 old tuberculin was negative. A roentgenogram of the skull was noncontributory. A roentgenogram of the chest revealed an irregular, mottled density involving the lower half of the right lung field, being more dense near the cardiac shadow (Fig. 4). The trachea was in the mid-line. The bronchovascular markings were slightly increased throughout the remaining portion of the lung fields. The heart was normal in size and position. Stool and blood cultures were negative for B. dermatitidis.

On May 17, 1949, iodide therapy in very small doses and desensitization with B. dermatitidis vaccine were begun concurrently. One drop of potassium iodide solution was administered orally three times daily and was to be increased by one drop per dose per day. The patient was given 0.1 cc. of heat-killed B. dermatitidis vaccine subcutaneously in a dilution of 1: 1,000. Injections were given every other day and were increased by

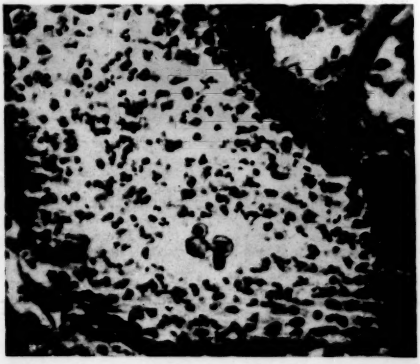


Fig. 3.—Cutaneous abscess showing budding Blastomyces dermatitidis (× 350).

0.1 cc. until a total single dosage of 1 cc. was reached; then a similar series of injections was again started with 0.1 cc. of a 1: 100 dilution. Two additional series of injections with the same increment of dosage were given, and the last injection was administered on July 20, 1949. Two additional injections of 1 cc. each of the undiluted vaccine were given subcutaneously within the next two weeks.

Two lesions over the eyelids and one over the nose were removed by excisional biopsy. The remaining lesions were treated with superficial x-ray therapy. A total of 1,300 r was administered over a period of six weeks. The single dosages never exceeded 100 r. The machine factors for irradiation consisted of 100 kv., 5 ma., both inherent and added filtration totaled 3 mm. of aluminum, and the half-value layer was 2.6 mm. of aluminum.

On Aug. 8, 1949, after 12 hr. of labor, a normal male infant was delivered at term, weighing 6 lb. 7 oz. (2,917 gm.). The delivery was spontaneous and uneventful. The baby appeared perfectly normal. His skin was clear. A cord serologic test for syphilis was negative. The chest was normal on roentgen examination. Gross and microscopic examinations revealed the placenta to be normal. Cultures from the placenta were negative for B. dermatitidis. The infant was never breast fed.

Both mother and child were discharged on Aug. 17, 1949. All the mother's cutaneous lesions had healed, and at the time of discharge she was requested to continue taking 35 drops of potassium iodide solution three times daily.

On July 11, 1950, almost a year later, neither mother nor child presented any discernible manifestations of blastomycosis. The mother had continued to take potassium iodide solution. Other studies at the time of her last examination showed the following results: the urinalysis was negative; the corrected sedimentation rate showed a fall of 41 mm. per hour; the white

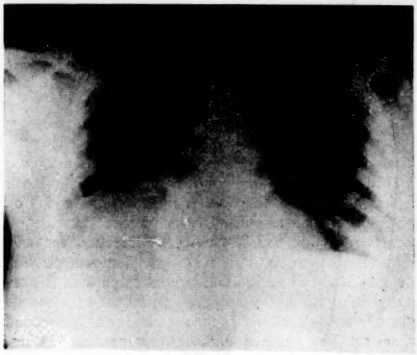


Fig. 4.—Roentgenogram of the chest six weeks after onset of pulmonary symptoms. An irregular, mottled density involved the lower half of the right lung field, being more dense near the cardiac shadow.

blood cell count was 3,900, with a differential formula of 29 lymphocytes, 2 monocytes, 67 polymorphonuclear neutrophils, 1 eosinophil and 1 stab form; the red blood cell count was 4,110,000; the hemoglobin determination was 11.5 gm. (method of Haden-Hausser); a Kahn serologic test for syphilis was nega-

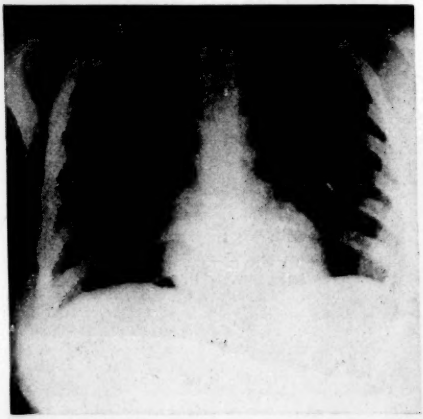


Fig. 5.—Roentgenogram of the chest 13 mo. after institution of therapy. The right lung field has cleared.

tive. Roentgen reexamination of the chest revealed no evidence of infiltration, and the findings in the lungs were within normal limits (Fig. 5).

On Oct. 7, 1949, x-ray films of the infant's chest again showed no abnormality.

The results of immunologic studies are shown in the table.

V 147
1951

COMMENT

The mother was given iodide therapy for more than one year, with approximately 35 drops of potassium iodide solution being administered three times daily during the entire period. At the end of this time she appeared well clinically, but continued to have an elevated sedimentation rate. At the time therapy was begun the mother had a positive intradermal reaction to B. dermatitidis vaccine and the complement-fixation test was positive. Three months after beginning therapy the patient gave birth to a normal infant. One year later the intradermal test on the mother continued to show a positive reaction. The complement-fixation test became negative at one time during the year, but shortly thereafter was again found to be positive. In view of Smith's studies this would indicate an unfavorable prognosis for the patient.[2]

At birth the infant had had a negative reaction to intracutaneous B. dermatitidis vaccine, but a positive complement-fixation reaction. No clinical lesions attributable to blastomycosis could be found.

At the end of the first year the infant continued to be clinically normal in every respect.

Immunologic Studies

Mother Date	Test: Intracutaneous*	Test: Complement-Fixation
5-11-49	3+ 48 hr.	.....
5-13-49	.....	1:4 dilution 3+
8- 8-49	.....	1:8 dilution 2+
3- 7-50	.....	Negative
6-30-50	.....	1:4 dilution 2+
7-11-50	2+ 48 hr.	.....

Infant Date	Test: Intracutaneous†	Test: Complement-Fixation
8- 8-49	.....	1:4 dilution 3+
8- 8-49	.....	1:8 dilution 2+
8-12-49	Negative	.....
11- 4-49	.....	Negative
3- 7-50	.....	Negative

* 0.1 cc. 1:1,000 heat-killed B. dermatitidis vaccine.
† 0.1 cc. 1:10,000 heat-killed B. dermatitidis vaccine.

To our knowledge this is the first example of blastomycosis in which passive transfer of complement-fixation antibodies from the mother has been demonstrated. Within three months after birth these antibodies spontaneously disappeared from the infant's blood.

SUMMARY

The clinical manifestations of a case of systemic blastomycosis complicated with pregnancy are presented.

The patient delivered a normal infant four and one-half months after she manifested signs and symptoms of systemic blastomycosis and three months after being placed under therapy for the disease.

The child appeared normal at birth and has remained so for one year. Passive transfer of complement-fixing antibodies from the mother was demonstrated immediately after birth; these antibodies disappeared from the infant's blood within the following three months.

Professional Proficiency.—There are two important and essential steps toward the maintenance of a physician's professional proficiency. One is to attend good general medical meetings which serve as refresher courses and broaden the knowledge of medicine. The second is to read good medical journals, bearing in mind that articles appearing in today's journals compose tomorrow's books.—Curtice Rosser, M.D., *Southern Medical Journal*, June, 1951, p. 563.

SILICON GRANULOMA OF SKIN DUE TO TRAUMATIC SAND INOCULATION

Julius E. Ginsberg, M.D., Chicago
and
Leonard A. Becker, M.D., Hines, Ill.

Silicon granulomas of the skin have been reported not infrequently in the English medical literature,[1] but, to our knowledge, they have not heretofore been described in a popular American medical periodical.[1a]

Silicon granulomas of the viscera, due to the use of talc on surgical gloves, have also been reported,[2] and this has led to the development for surgical use of powders containing no silicon.

Cutaneous silicon granulomas due to traumatic silicious inoculation of the skin are probably not too uncommon in this country, but simply are not recognized. The lesions are prone to occur about the face and exposed portions of the extremities that are subject to earthen trauma. Among the types of injuries causing these late-

Fig. 1.—*A*, appearance of the flesh-colored granulomas before treatment with aureomycin and vitamins was started. The dark spots at the base of the neck are biopsy wounds. *B*, appearance of the patient Oct. 30, 1950. The skin-colored granulomas flattened, and a slight pigmentation remained. The skin appeared almost normal in February, 1951.

appearing skin-colored growths are those associated with cycling and mountaineering, and even ordinary falls on sandy or flinty roads or paths. The sand particles are actually bruised into the skin during the fall.

Clinically these lesions are apt to be misdiagnosed as hypertrophic scar, keloid, Boeck's sarcoid, or lichenoid tuberculid.[3]

These granulomas of the skin may appear as much as two to 29 years after traumatic inoculation of the skin with sand.[1] The long latent period following trauma be-

From the Department of Dermatology, Northwestern University Medical School, and the Department of Dermatology, Veterans Administration Hospital, Hines, Ill.

Published with the approval of the Chief Medical Director, Veterans Administration. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Sommerville, J., and Milne, J. A.: Pseudo-Tuberculoma Silicoticum: A Form of Cutaneous "Sarcoid," Brit. J. Dermat. **62**: 105 (March) 1950.

1a. Additional references, particularly in the specialty journals, have come to our attention since submitting this paper for publication.

2. Sellig, M. G.; Verda, D. J., and Kidd, F. H.: Talcum Powder Problem in Surgery and Its Solution, J. A. M. A. **123**: 950 (Dec. 11) 1943.

3. Ockuly, O. E., and Montgomery, H.: Lichenoid Tuberculid, J. Invest. Dermat. **14**: 415 (June) 1950.

fore the lesions appear also accounts for the paucity of reports of them, probably because of failure to obtain a history which associates the ancient injury with the origin of the tumor. Use of the polarizing microscope, which is available in almost all pathology laboratories, facilitates microscopic diagnosis when a biopsy specimen is examined.

REPORT OF A CASE

D. P. P., a white man aged 28, was first seen by us in March, 1950. At that time he had multiple, shiny, flesh-colored and pink, papular and nodular, soft lesions over the right side of the face and neck, the right deltoid area, and the dorsum of the second and third fingers of the left hand.

This eruption had begun only four months previously on a skin which had heretofore been normal except for occasional acne lesions. The first lesion had appeared below the right ear, the others developing in clusters elsewhere shortly thereafter.

The patient felt that the lesions were related to an injury he sustained while in the service in April, 1943. While undergoing training during an infiltration course, a small land-mine exploded just ahead and slightly to the right of him. At the moment, he was crawling along on his knees, abdomen, and elbows, with his rifle cradled in his arms. He was wearing standard cotton fatigues and a steel helmet with the chin strap hooked over the point of the chin. He felt that the protection by the chin strap accounted for the lack of lesions along the right mandible. In addition to sustaining multiple perforating wounds of the skin from flying particles of sand and dirt, both tympanic membranes were ruptured and he was unconscious for about six hours. He further stated that for a period of about three weeks following the injury the wounds were probed daily and numerous foreign particles were removed, primarily from the right side of the face and neck.

Fig. 2.—Low-power photomicrograph of biopsy specimen showing granuloma replacing most of the dermis. The tears in the dermis are due to silicon particles being drawn through the section by the microtome blade.

In about six weeks all of the wounds were apparently healed, and only a few small "blue spots" remained. His wife noticed that some of these "blue spots" were still present when the "lump" appeared below his right ear. Up to two years prior to our first observation, grains of sand were extruded periodically from his face and neck while shaving, primarily from the right side and more from the neck than from the cheek. He also said that, since his injury, he had had no more acneform lesions on the right side of his face and neck than on the left.

There was no history of a similar condition in other members of his family.

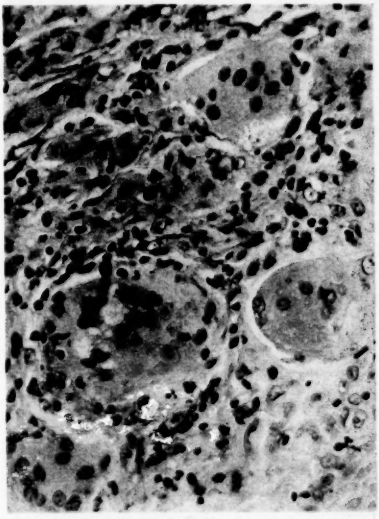


Fig. 3.—Higher power photomicrograph of Fig. 3, showing vacuolated foreign body giant cells, epithelioid cells, fibroblasts, and other cells. The vacuoles in the giant cells were not doubly refractile

Physical examination, except for the lesions described above, was essentially normal, and the patient was in good general health. The lesions showed no signs of necrosis and were symptomless. An apple-jelly color was seen with diascopic pressure of the lesions.

Routine laboratory studies, chest x-ray, and x-ray examination of the bones of the feet and hands were essentially normal except for a "pseudocyst of the left carpal navicular, not believed to represent evidence of sarcoidosis." First strength tuberculin test was strongly positive. Smear, culture, and guinea pig inoculation from aseptically obtained biopsy specimens were all negative.

Histopathological studies revealed the following. The epidermis showed loss of rete processes. A dense infiltrate of giant cells, epithelioid cells, and lymphocytes was separated from the epidermis by a narrow band of collagen fibers and extended deep into the dermis, almost entirely replacing the collagen in these areas. Stain for acid-fast bacilli was negative. With the use of a polarizing microscope, doubly refractile crystalline bodies were seen in biopsy specimens taken before and after aureomycin therapy.

For about two months following our first observation of the patient on March 3, 1950, there was a gradual increase in the number of lesions in the above-mentioned areas as well as on the fingers of the right hand. During this time no local or systemic treatment was administered. From June 26 to July 10, 1950, he was given aureomycin, 250 mg., orally four times daily. From July 10 to July 19, and again from Sept. 22 to Oct. 16, he was given aureomycin, 250 mg., three times daily. Two or three times daily during these periods aureomycin ointment was applied to the face and neck. He was also given therapeutic formula vitamins during the periods of aureomycin therapy. After a week of aureomycin therapy there was a noticeable improvement, and from that time on gradual regression of the lesions continued, as shown in the illustrations.

V 14
1951

COMMENT

Silicon granulomas of the skin ordinarily do not undergo spontaneous involution. It would seem that the improvement coincident with aureomycin and therapeutic formula vitamin therapy would indicate this therapy was of value and that the improvement was not attributable to spontaneous improvement. If this is the case, the improvement may be explained on the basis of the effect of these medications on associated undetermined infection. Silicon particles could still be demonstrated in healed lesions with the polarizing microscope.

The microscopic changes seen in silicon granulomas of the skin resemble those described in beryllium (a similar foreign body) granulomas of the skin,[1] granulomatous changes described for talc (magnesium silicate) granulomas of the viscera,[2] and asbestosis [3] (asbestos is

Fig. 4.—Brighty refractile silicon particles in the granuloma tissue as demonstrated with the polarizing microscope.

composed chiefly of magnesium silicate). The polarizing light microphenomena are not present in the latter conditions.

826 E. 61st St.

4. Dutra, F. R.: Beryllium Granulomas of Skin, Arch. Dermat. & Syph. **60**: 1140 (Dec.) 1949.
5. Gardner, L. U., and Cummings, D. E.: Experimental Asbestosis, abstracted in Am. Rev. Tuberc. **25**: 60 (May) 1932.

Metabolism and Catabolism.—Metabolism is the term employed to embrace the various chemical processes occurring within the tissues upon which the growth and heat production of the body depend and from which the energy for muscular activity and for the maintenance of vital activity and of vital functions is derived. Catabolism is the term applied to those reactions which involve the breakdown or decomposition of substances into their simpler constituents. Anabolism is the word used to connote building up or assimilative processes.—Charles Herbert Best, M.D., and Norman Burke Taylor, M.D., The Physiological Basis of Medical Practice, Baltimore, The Williams & Wilkins Company, 1950, p. 607.

BENIGN HISTOPLASMOSIS IN SIBLINGS

REPORT OF CASES

Isidore Rod Miller, M.D.
and
Solomon Grossman, M.D., New York

The literature in the past few years has emphasized the more recent interpretations of pulmonary calcifications, both parenchymal and hilar. The more widespread use of the Mantoux test, with the increase in negative reactors, revealed the fallacy of considering all the lesions tuberculous. More attention given the history, physical examination and laboratory findings results in the discovery of pathological findings simulating tuberculosis but of other etiology. The commonest are the fungus infections, namely, coccidioidomycosis and histoplasmosis. In the presence of negative tuberculin tests, these two diseases must be included in differential diagnosis regardless of the patient's age or geographical location.

In this report we are concerned with histoplasmosis, which is no longer considered a tropical disease. The incidence of histoplasmosis has increased generally in temperate and subtropical areas. Statistics show that males are more often affected, and that persons of all ages are susceptible although more cases appear in children. The portal of entry has not yet been finally determined, though it appears that the mouth is probably the most frequent site. A number of public health surveys revealed that the states with the highest incidence of histoplasmin sensitivity also have the greatest number of cases of pulmonary calcification. Calcification is two to four times as frequent in the histoplasmin reactors as in the tuberculin reactors. The positive histoplasmin reactions have been noted oftener in persons residing in rural areas. Geographically, the trend of the incidence of tuberculin sensitivity was the reverse of that for histoplasmin. The skin tests with histoplasmin are of greatest value in epidemiologic studies of primary or sensitizing infections. In persons with late disseminated histoplasmosis the skin tests may be negative.

Furcolow,[1] in a study of 72 asymptomatic cases in school children in Kansas City, reported the roentgenologic characteristics of persistent pulmonary infiltrations found in histoplasmin-positive and tuberculin-negative cases. Three cases had hilar or mediastinal adenopathy without parenchymal involvement. Three cases showed multiple, widely disseminated lesions occupying both lung fields. Seventeen cases showed pneumonic infiltrations usually consisting of a small area of infiltration with poorly defined borders. In 49 cases the lesions were sharply circumscribed nodular shadows. These children have been followed for periods up to four years, during which time some of the infiltrates disappeared completely, some became fibrotic, but in the majority calcification gradually developed.

From the Bureau of Tuberculosis, New York City Department of Health.

1. Furcolow, M. L.; Mantz, H. L., and Lewis, I.: The Roentgenographic Appearance of Persistent Pulmonary Infiltrates Associated with Sensitivity to Histoplasmin, Pub. Health Rep. **62**: 1711 (Dec. 5) 1947.

White and Hill [2] reported a tendency to familial occurrence. They observed 11 cases of disseminated pulmonary calcification in four family units.

We are reporting two cases of benign histoplasmosis in Negro brothers which illustrate some of the problems in diagnosis.

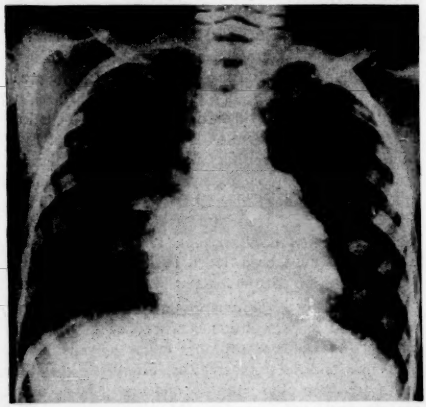


Fig. 1.—Chest x-ray of L. K., aged 6 yr., taken Jan. 9, 1950. Calcified nodules throughout both lungs are revealed.

REPORT OF CASES

CASE 1.—L. K., aged 6 yr., had a survey chest film taken on Jan. 9, 1950 (Fig. 1), which revealed calcific nodules disseminated throughout both lung fields. Tuberculin tests were negative up to 1:100 dilution; histoplasmin test was positive in 1:1,000 dilution. The complement-fixation test for histoplasmosis was positive in undiluted serum.

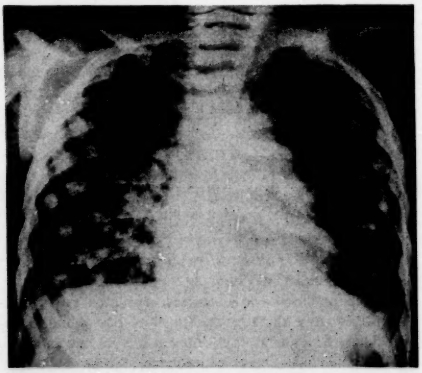


Fig. 2.—Chest x-ray of L. K. at age of 4½ yr. Fuzzy, mottled infiltration throughout both lungs can be seen.

Eighteen months previously the patient had spent six weeks in Mississippi. He became ill and during the last two weeks of his stay a high fever, cough, and epigastric tenderness developed. A diagnosis of malaria was made and quinine given. He was brought back to New York and was taken to a local clinic for examination on Aug. 26, 1948. Temperature was 98 F., hemoglobin 65%, white blood cells 5,000, with a differential of 52% polymorphonuclear cells, 42% lymphocytes, 3% monocytes, and 3% eosinophils. A chest x-ray (Fig. 2) revealed a fuzzy infiltration throughout both lungs. A diagnosis of miliary tuberculosis was made. The youngster did not return for further examination because his symptoms disappeared. He had had a chest x-ray which was negative at the same clinic on Nov. 12, 1947. A tuberculin patch test at this time was also negative.

CASE 2.—O. K., aged 3 yr., had a survey chest film taken on Jan. 9, 1950 (Fig. 3), which revealed a large left paratracheal density. Tuberculin tests were negative up to 1:100 dilution; histoplasmin test was positive in 1:1,000 dilution. The complement-fixation test for histoplasmosis was negative.

Eighteen months previously he had spent six weeks in Mississippi. During the last two weeks of his stay high fever, cough, and epigastric tenderness developed. A diagnosis of malaria was made in his case also and quinine was given. He was brought back to New York. He had no symptoms after he returned to New York, and had no examination until his survey x-ray taken on Jan. 9, 1950.

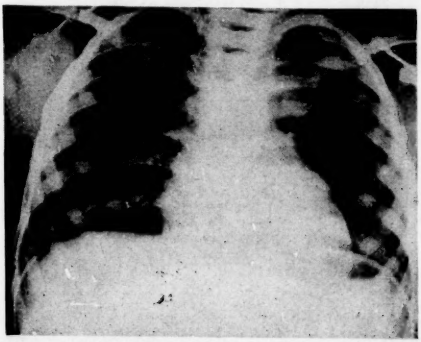


Fig. 3.—Chest x-ray of O. K., aged 3 yr., taken Jan. 1, 1950, showing left paratracheal density.

COMMENT

The principal significance of the benign form of histoplasmosis is that it so closely resembles tuberculosis. The pulmonary infiltrations and calcifications are similar in both diseases. In the past, the presence of calcification in a chest x-ray was taken as an indication of a tuberculous infection. A negative tuberculin reaction occurring in patients with calcified lesions was explained as a loss of allergy due to a healed process or anergy. Recent work [3] has shown that in the desert areas of the Southwest coccidioidin tests gave positive reactions in many cases of pulmonary calcification with negative tuberculin tests. In the Mississippi Valley regions, histoplasmin tests gave positive reactions in cases of pulmonary calcifications with negative tuberculin tests. Tuberculin testing alone is, therefore not sufficient in patients with pulmonary lesions.

SUMMARY

The chest x-rays of two Negro brothers, 6 yr. and 3 yr. of age, are presented. The x-rays showed calcified nodules in the older boy and a mediastinal density in the

2. White, F. C., and Hill, H. E.: Disseminated Pulmonary Calcification, Am. Rev. Tubercl. 62:1 (July) 1950.

3. Palmer, C. E.: Nontuberculous Pulmonary Calcification and Sensitivity to Histoplasmin, Pub. Health Rep. 60:513 (May 11) 1945. Furcolow, M. L.: Development of Calcification in Pulmonary Lesions Associated with Sensitivity to Histoplasmin, Pub. Health Rep. 64:1363 (Nov. 4) 1949.

V 14
1951

younger. Skin reactions were positive to histoplasmin and negative to tuberculin. The benign form of histoplasmosis was diagnosed in these brothers by demonstrating pulmonary infiltrations and calcifications, and a positive skin reaction to histoplasmin in the absence of evidence of tuberculosis.

333 E. 80th St., 21 (Dr. Miller).

PAPILLOMA OF THE UMBILICUS

Sidney Vernon, M.D., Duluth, Minn.

Ficarra [1] recently reported a case of umbilical papilloma, referring to Reder's [2] report of the 13th case and to 12 cases in Cullen's [3] textbook "Diseases of the Umbilicus." This entity has not been frequently reported. The following clinical report is presented as the 15th recorded case.

Umbilical papilloma is not a serious condition, but presents a diagnostic problem. Embryology of the area shows that urachal anomaly, or a vitelline duct vestige may occur. Connection with the urinary tract and with the gastrointestinal tract must be ruled out. The gross appearance of epithelial abnormality may suggest possible malignancy. The problem is illustrated in this report.

REPORT OF CASE

J. T. C., a 13-yr.-old girl, was admitted to the hospital on Jan. 13, 1947, complaining of "drainage around the navel." This condition had been present for three weeks, and at first when the discharge was profuse it was accompanied with nausea and pain about the umbilicus. The patient's mother stated that healing of the cord at birth seemed prolonged.

The family history was essentially noncontributory. The past history showed the usual childhood diseases. At the age of 5 yr. the patient had diphtheria with one year's hospitalization, and at the age of 10 yr. had three weeks' hospital observation for a head injury.

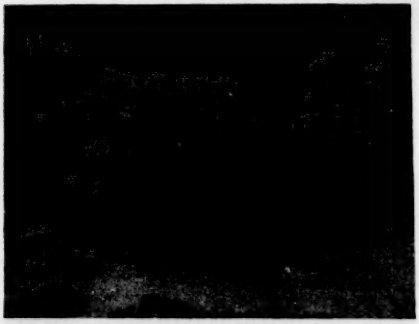


Fig. 1.—Cross section of tumor showing papillary growth.

Examination revealed a healthy child with normal findings except for a few large anterior cervical glands. Blood pressure was 105/58. The umbilicus showed a dark, discolored, granulomatous, nontender area, slightly raised, cracked and firm, with a serous yellow exudate. The surrounding area for 2 mm. was red and inflamed. No nearby masses were felt. The circumumbilical area was probed with a ureteral catheter and no tracts were found.

The patient was given methylene blue orally for two days. No dye appeared around the umbilicus, although the urine was deeply stained. Later she was given carmine red chalk by mouth. No dye appeared about the umbilical area. These tests showed there was no connection between the umbilical area and the urinary or intestinal tracts. A biopsy was taken.

Fig. 2.—Round epithelial pearls are not indicative of malignancy. Predominant cells are prickle cells (stratum mucosum). Pigmented columnar basal cells in polygonal pattern are noted in the stratum germinativum. These surround bood vessels and connective tissue and are the result of previously formed granulation tissue.

The biopsy revealed that in sections there were interconnecting sheets of stratified squamous epithelium surrounding a delicate vascular stroma. Several mitotic figures were seen in the stratum mucosum, and in a few areas the stratum germinativum appeared disrupted and extended irregularly into the stroma. These areas suggested the possibility of malignant change in the tumor. The diagnosis was papilloma.

Beta hemolytic Streptococcus was cultured from the periumbilical area. Urine specimens on different days were normal. The serology was normal. Blood study showed hemoglobin 84%, white blood cells 9,500, with 31% neutrophils, 58% lymphocytes, 10% eosinophils and 1% monocytes. Culture from the umbilicus was negative for Mycobacterium tuberculosis.

Roentgen study of the gastrointestinal tract revealed no abnormality. No periumbilical sinus deep enough for lipiodol* study was found. The radiologist believed that x-ray therapy was not indicated because of the benign nature of the condition. The urologist expressed the opinion that there was no connection with the urinary tract and advised surgical excision.

Operation was performed on Feb. 5, 1947, under gas-oxygen-ether anesthesia. Block excision was favored because of the possibility of malignancy of the papilloma. A horizontal, wide elliptical incision 4 in. (10 cm.) long with a 1½-in. (3.8 cm.) margin on each side of the lesion was made. The cut skin edges were sewed over the tumor. Dissection was continued to the sheath of the rectus where horizontal incisions were made. En masse dissection continued to the peritoneum, and the mass was removed. The peritoneum was not opened. Bleeding was thoroughly controlled. The rectus muscle was brought together in the mid-line, and the anterior sheath was imbricated. After placing subcutaneous sutures, the skin was closed with an intracuticular suture. Gross examination of the specimen showed no invasive tendency, and it was obvious that all of the tumor had been excised.

The pathologist reported that the epithelium was elevated and thrown into papillary projections. The projections were covered

1. Ficarra, B. J.: Papilloma of the Umbilicus, Am. J. Surg. 79: 607-609 (April) 1950.
2. Reder, F.: Nonmalignant Papilloma of the Umbilicus, Ann. Surg. 87: 636-637, 1928.
3. Cullen, T. S.: Diseases of the Umbilicus, Philadelphia, W. B. Saunders Company, 1916, pp. 360-365.

by epithelium of normal thickness and had a connective tissue core. A thick layer of keratin covered the entire tumor. Beneath this area the elongated rete pegs were thrown into intricate lacy folds interrupted by loose connective tissue. Some of the rete pegs contained small pearls of keratin. A heavy infiltrate of lymphocytes was noted in the subcutaneous tissue.

Most of the squamous cells were derived from the prickle-cell layer (stratum mucosum). Small islands of basal-cell proliferation and of keratin formation were seen in the middle of rete pegs. A moderate amount of pigmentation was noted in the basal-cell layer (stratum germinativum). There was no evidence of neoplasia and no embryonic structures were seen. The diagnosis was squamous papilloma.

The patient was discharged 11 days after the operation.

COMMENT

Etiology is a matter of speculation. If exuberant granulation on the umbilical wound is closely followed in the healing process by inward migration of the epithelial border of skin, a papilloma may result. Factors controlling the architecture of reparative growth operate minimally at the umbilicus.

Surgery is indicated because of the possibility of cancer, since both gross and microscopic appearances are suggestive of malignancy. The added difficulties of local hygiene with an abnormal umbilicus also indicate surgical correction. The lesion commands attention when infection is superimposed on it, and probably is otherwise ignored. Infection increases the growth potential of the lesion and presents the possibility of carcinoma. This case is reported because the condition is apparently uncommon.

5601 Grand Ave.

TURBAN TUMORS

REPORT OF A CASE

George J. Coloviras Jr., M.D., Detroit
and
Richard E. Gery, M.D., Lafayette, Ind.

The appearance of a patient with turban tumors is so extraordinary that it leaves a permanent impression on all observers. Few cases have been reported, and the majority of these are from the foreign literature. Cooper [1] estimates that a total of less than 50 cases have been reported.

There is a typical picture of this disease. The lesions usually occur on the scalp. The grapelike tumors are usually pink or maroon in color and often are present with a pedicle, which appears easy to excise; such, of course, is a delusion. The tumors vary in size from that of a quarter to much larger proportions, varying from 4 by 6 by 3 cm., both single and multiple. There seems to be no particular diagnostic test other than biopsy. These tumors feel like gum rubber balls when palpated and are prone to hemorrhage and ulceration. There is a definite familial involvement, most often in more than one member of a family. The onset of growth is at puberty, and growth is slow. Benignity would appear to be the tendency, inconvenience the commonest complaint. The distribution is mostly over the head (turbanlike), but the lesions also occur over the trunk, back, and extremities.

This tumor was first reported by Ancell [2] in 1842. Various authors described it as a cylindroma,[3] while Spiegler [4] in 1895 described it as a perithelioma. Frieboes [5] seems to have made the most accurate analysis of these tumorlike masses, concluding that they were of epithelial tissue of slow growth. Ronchese [6] believed the tumors originated in the sebaceous glands, while others [7] believed they originated from surface epidermis or hair follicles. Savatard [7a] coined the term "epithelioma adenoides cysticum." Gabarro [7] reported the largest specimen successfully removed and further adopted Savatard's nomenclature. Ormsby [8] further separated epithelioma adenoides cysticum from cylindroma mainly on hereditary factors, development of cystic structures, and size of the lesions. Sachs [9] reported an interesting case in a Negro, although the growth appeared to be a multiple tumor and not strictly a single type. Ormsby [8] also reported a combination of the two tumor types.

REPORT OF A CASE

History.—This patient first noted a lump on her head when she was about 35 years of age. This tumor grew to the size of a hen's egg, and within five years she had had four tumors excised. At the age of 50 she was admitted to St. Elizabeth Hospital, Lafayette, Ind., and several more tumors were removed. The tumors were allowed to grow after this attack, and by late 1949, when the patient was 64, she experienced a minor hemorrhage from one of the pedunculated tumors. This precipitated her arrival at the hospital in early 1950, at which time 27 tumors varying in size from that of a dime to that of an orange were removed from the scalp. The patient was discharged and readmitted in May, 1950, for further treatment of the tumors after a suitable period of preparation had been carried out. At the time of this admission she appeared to be in better condition, although there was not much change in the appearance or size of the tumors.

The patient's father, who died at the age of 74, had had a tumor of the forehead, which was accidentally excised by an icicle and did not recur. Her mother died at the age of 65 of unknown cause. The siblings did not have anything resembling these tumors.

The pertinent facts of the patient's past history are as follows: at age 35 one tumor was removed; at age 40 four tumors were removed; at age 50 numerous tumors were removed; on the first admission at the age of 64 some 27 tumors were removed, and on the second admission at the age of 64 some 12 tumors were removed.

Physical Examination.—The patient was an elderly woman, not in great pain but acutely distressed with her appearance and

The illustrations accompanying this study were taken by J. MacKenzie, Department of Medical Photography, St. Elizabeth Hospital, Lafayette.

From the Department of Thoracic Surgery, the Herman Kieffer Hospital and formerly Resident Surgeon, St. Elizabeth Hospital, Lafayette, Ind. (Dr. Coloviras) and Attending Surgeon, St. Elizabeth Hospital (Dr. Gery).

1. Cooper, D. L.: Cylindroma: Report of Unusually Extensive Case, J. A. M. A. **132**: 575-577 (Nov. 9) 1946.

2. Ancell, H.: History of a Remarkable Case of Tumours, Developed on the Head and Face, Accompanied with a Similar Disease in the Abdomen, Med.-Ch. Tr. **25**: 277, 1842.

3. Pinkus, F.: Arch. f. Dermat. u. Syph. **138**: 342, 1922.

4. Spiegler, E., cited by Sachs, W., and Sachs, P. M.: Turban Tumors: Report of a Case with Unusual Pathologic Findings, Including Both Epidermal and Dermal Nevi, Arch. Dermat. & Syph. **42**: 15-22 (July) 1940.

5. Frieboes, W., cited by Sachs, W., and Sachs, P. M.[4]

6. Ronchese, cited by Savatard.[7a]

7. Gabarro, P., and Baker, S. L.: Enormous Epithelioma Adenoides Cysticum of the Scalp, with Pathological Report, Brit. J. Surg. **33**: 188-190, 1945.

7a. Savatard, L.: Early Epithelioma of the Skin, Brit. J. Dermat. **34**: 381-396, 1922.

8. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 747.

9. Sachs, W., and Sachs, P. M.: Turban Tumors: Report of a Case with Unusual Pathologic Findings, Including Both Epidermal and Dermal Nevi, Arch. Dermat. & Syph. **42**: 15-22 (July) 1940.

V 14
1951

the odor emanating from her head. The head was covered with a blood-streaked towel. When the towel was removed, innumerable masses of pedunculated tumors varying in size from peas to small oranges could be seen. These tumors, where approximal, showed signs of ulceration and hemorrhage with resultant offensive odor. One tumor on the side of the head had a covering

Fig. 1.—Numerous egg-size masses are evident

of blood clot indicating a recent hemorrhage. There were small nodular lesions in the ears and on the forehead. There were no tumors in the neck, and the thyroid could not be palpated. There was a chain of pea-sized tumors down the right side of the midback. There were no masses in the abdomen or in the skin of the abdomen. Cardiovascular and genito-urinary examinations were noncontributory. There were two subcutaneous nodules on the right arm, with larger masses symmetrically positioned on the left arm. These masses were pealike in size. There was one other mass on the left midthigh.

Hospital Course.—This patient was admitted as already outlined, and numerous tumors were excised in three stages. It was felt that because of the advanced age of the patient a complete

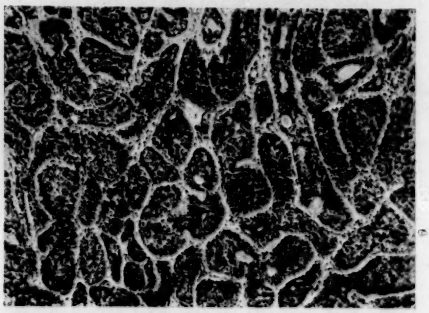


Fig. 2.—Typical nests of cells, well surrounded with heavy collagen.

removal by "scalping" with immediate skin grafting was not the method of choice, and a piecemeal excision program was undertaken. The accompanying illustration was made after the first two stages had been completed and the third stage was to begin. The tissue was excised and sectioned, and the pathological tissue revealed a neoplasm composed of various sized nests of epithelial cells, the cell nests being separated by strands of collagenic connective tissue, which completely encircled them. The individual cells were small, with a dark nucleus, and were consistent in appearance with basal cells, and showed palisading at the periphery of the cell nest. In some instances the cell nests appeared cystlike, the center being filled with an amorphous eosin-staining material. The overlying epidermis was stratified, squamous in type, and without abnormality in type except for being somewhat atrophic. There was no appearance of malignancy (Fig. 2).

It is planned to continue the excision of these tumors until the scalp is almost clean and then to complete a series of skin grafts where indicated.

CONCLUSION

A further case of turban tumors is reported.

1151 Taylor Ave.

APLASIA OF THE BONE MARROW DURING MESANTOIN® THERAPY

REPORT OF A FATAL CASE

Elliot Witkind, M.D.
and
Margaret E. Waid, M.D., Newark, N. J.

Mesantoin® (3-methyl-5,5 phenylethyl hydantoin) has received widespread acclaim as an anticonvulsant drug particularly useful in convulsive states of the grand mal and psychomotor types.[1] The early investigators reported few toxic manifestations of the drug.[2] However, since 1946, several severe hematological reactions with recovery [3] and six cases which terminated fatally [4] have appeared in the literature. Trimethadione (tridione®) as well as mesantoin®, was implicated in the fatality reported by Harrison, Johnson and Ayer.[4c]

The object of this paper is to report a fatal case of aplasia of the bone marrow directly attributable to mesantoin® idiosyncrasy and to review the toxic manifestations of this relatively new and valuable anticonvulsant preparation.

REPORT OF CASE

Mrs. A. V., a 35-yr.-old white woman, was admitted to the medical service of the Newark City Hospital complaining of sudden onset of nonmigratory joint pains of two days' duration involving the ankles and knees. Within a few hours after onset

Former medical resident and resident in pathology (Dr. Witkind) and resident in pathology (Dr. Waid).
From the "A" medical service, the Department of Pathology of Newark City Hospital, and the Office of the Chief Medical Examiner, Essex County, N. J.

1. Kozol, H. L.: Treatment with a New Drug: 3-Methyl 5,5-Phenyl-Ethyl-Hydantoin (Phenatoin), Am. J. Psychiat. **103**: 154-158 (Sept.) 1946.

2. Kozol,[1] Lennox, W. G.: Two New Drugs in Epilepsy Therapy, Am. J. Psychiat. **103**: 159-161 (Sept.) 1946.

3. (*a*) Frank, C. W., and Holland, J. F.: Pancytopenia from "Mesantoin," J. A. M. A. **138**: 1148-1150 (Dec. 18) 1948. (*b*) Bloom, N.; Lynch, J. P., and Brick, H.: "Mesantoin" Poisoning with Aplastic Anemia and Recovery, J. A. M. A. **138**: 498-499 (Oct. 16) 1948. (*c*) Davies, R. R.; Fisch, C., and Tischer, P. E.: Pancytopenia Due to Mesantoin: Report of a Case, New England J. Med. **242**: 863-864 (June 1) 1950.

4. (*a*) Frank and Holland.[3a] (*b*) Aird, R. B.: The Treatment of Epilepsy with Methylphenylethyl Hydantoin (Mesantoin), California Med. **68**: 141-146 (March) 1948. (*c*) Harrison, F. F.; Johnson, R. D., and Ayer, D.: Fatal Aplastic Anemia Following Use of Tridione and a Hydantoin, J. A. M. A. **132**: 11-13 (Sept. 7) 1946. (*d*) Weller, R. W., and Metcalfe, J.: Fatal Pancytopenia Following Use of "Mesantoin": Report of a Case, New England J. Med. **241**: 17 (July 7) 1949. (*e*) Best, W. R., and Paul, J. T.: Severe Hypoplastic Anemia Following Anticonvulsant Medication: Review of the Literature and Report of a Case, Am. J. Med. **8**: 124-130 (Jan.) 1950.

of joint pains she had developed spontaneous ecchymosis over her abdomen, lower back, buttocks, and extremities; profuse vaginal bleeding, coinciding with her expected date of menstruation; epistaxis; oozing gums; nausea, and hematemesis. Prior to the occurrence of these fulminating symptoms the patient had noted moderate fatigue and generalized malaise during the past few months.

She had been in good health until the age of 23 when grand mal seizures began. Despite treatment with phenobarbital and diphenylhydantoin (dilantin®) sodium U.S.P. the attacks had persisted, although with less frequency. At no time had trimethadione been administered. She had had three pregnancies and had delivered normal infants; however, her last pregnancy, one year prior to admission, had been complicated by hemorrhage. Five months prior to admission all previous medications had been discontinued and administration of mesantoin® had been instituted in doses ranging from 0.1 to 0.4 gm. daily, with apparently dramatic diminution in the frequency of the attacks. During this period seizures of the Jacksonian type had been noted on several occasions, but only one grand mal episode occurred. The only untoward reactions were weakness, drowsiness, and malaise when the patient was taking 0.3 gm. of the drug daily. These symptoms had disappeared when the dose was reduced to 0.1 gm. per day and reappeared when it was increased to 0.4 gm. per day. This dose had been administered for one month prior to admission. A total of approximately 40 gm. had been ingested by the patient during the five-month period of treatment.

Blood Composition During Hospitalization

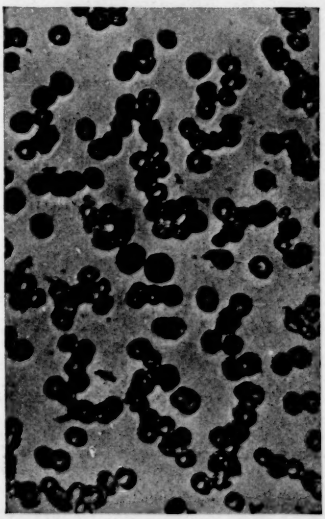
	Hospital Days					
	1	2	3	4	5	6
Red blood cells per cubic millimeter	2,480,000	2,100,000	2,550,000	.....	2,350,000	.....
Hemoglobin, gm./100 cc. (Sahli)	8.2	8.2	7.9	.....	8.6	8.5
White blood cells per cubic millimeter	1,350	1,300	1,700	.....	950	1,000
Differential						
Neutrophils, %	4	.....	4	.....	2	.....
Lymphocytes, %	96	.....	96	.....	98	.....
Platelets per cubic millimeter	60,000	.....	.....	.....	.....	20,000
Blood transfusions, cc.	500	400	250	250	700	1,000

Physical examination on admission revealed an acutely ill, apprehensive young woman with a temperature of 104.2 F., a pulse rate of 112, 24 respirations per minute, and blood pressure 105 systolic and 65 diastolic. There were pronounced pallor and small petechiae in the soft pallate; the gums were soft, friable, and bleeding, and continuous oozing from the vaginal orifice was noted. Scattered diffusely over the lower abdomen, buttocks, lumbar region, and extremities were multiple ecchymotic areas. The heart and lungs were normal. No abdominal masses were noted. The neurological examination and the remainder of the physical examination were negative.

Laboratory studies on admission showed a red blood cell count of 2,480,000 with a hemoglobin of 8.2 gm. per 100 cc. (Sahli), which remained fairly stable despite blood transfusions (table). The white blood cell count was 1,350 with 96% lymphocytes and 4% neutrophils. The platelet count varied from 60,000 per cubic millimeter (direct method) to 20,000 per cubic millimeter; the reticulocyte count was 0.4%, bleeding time three minutes 55 sec. (Duke's test), clotting time 4 min. 30 sec. (glass slide method), sedimentation rate 127 mm. after one hour (Westergren), hematocrit value 18 per 100 cc. Urine showed albuminuria and microscopic hematuria. The sternal marrow revealed 300 nucleated cells per cubic millimeter, no myeloid elements or megakaryocytes, a few bizarre normoblasts (6%), and plasma cells (6%). The majority (88%) of the cells were lymphocytes (figure). The Rumpel-Leede phenomenon was distinctly positive. A chest plate made on admission showed no abnormality.

Treatment consisted of multiple daily transfusions, 3.1 L. being administered during a period of six days, consisting of penicillin, streptomycin, crude liver extract, rutin, ascorbic acid, vitamin K, ferrous sulfate, Armour's yellow bone marrow preparation, intravenous glucose and protein hydrolysate. Despite these measures, the patient pursued a downhill course with fluctuating temperatures varying from 101 F. to 106 F. On the third hospital day, melena, severe rectal bleeding and gross hematuria appeared. During the next few days epistaxis, menorrhagia, hematemesis, purpuric skin lesions, and restlessness became progressively more pronounced. There was a gradual increase in the respiratory and pulse rate, and distant cardiac sounds were noted. On the sixth hospital day the patient lapsed into a coma, became moribund, and died.

At post-mortem examination, icterus of the skin and sclera, multiple ecchymotic areas of the chest, lumbar regions and extremities were noted. The gums were spongy, friable and hypertrophic with evidence of recent bleeding. Subepicardial petechiae and subcapsular hepatic hemorrhages were noted. A small pulmonary infarction was present in the right upper lobe. There were submucosal hemorrhages of the stomach, small and large intestines, renal pelvices, ureters and bladder. The uterine cavity contained a cast of clotted blood. The spleen was slightly enlarged and congested and weighed 225 gm. The bone marrow of the ribs, vertebras and sternum was pale pink and watery in appearance. Generalized subdural hemorrhage, most pronounced over the left frontoparietal region, with a 3-cm. area of cystic degeneration in the area of the left precentral gyrus, was found. Since the drug had been discontinued when the acute symptoms developed, toxicological studies were not performed.



Photomicrograph of sternal marrow. Note hypochromatic red blood cells, absence of thrombocytes, and severe depression of normal hematopoietic elements. Two lymphocytes are visible in this field.

Microscopic examination confirmed the submucosal hemorrhages of the gastrointestinal tract, bladder and uterus. Alveolar congestion, recent and old hemorrhage of the lungs, kidneys, spleen, and extravasation of blood into the cortical gray matter was evident.

COMMENT

This case illustrates the important early and most frequent toxic manifestations of mesantoin® which should not be minimized, namely, weakness, drowsiness, and generalized malaise. However, the appearance of these symptoms is not necessarily the precursor of the development of severe hematological reactions. The late symptoms were those related to increased bleeding ten-

V 14
1951

dencies, such as spontaneous ecchymosis, oozing gums, epistaxis, menorrhagia, hematemesis and joint pains.

A review of the literature reveals that, in addition, anorexia, nausea, vomiting, constipation, lethargy, fever, cervical lymphadenopathy, nystagmus, ataxia (rarely), headache, dizziness, nervousness, transient urticaria, gingival hypertrophy, sore throat and metrorrhagia, have been reported. Toxic psychosis was observed following ingestion of four tablets.[5] Various rashes, usually morbilliform in nature,[2] appear to be a frequent toxic manifestation appearing often within the first two weeks of treatment. Ruskin [6] reported one case of a scarlatiniform rash and a fulminating case of dermatitis bullosa medicamentosa which terminated fatally. The patient with the latter condition had dermal sensitivity to a variety of drugs.

Aplasia of the bone marrow, with resultant pancytopenia and hemorrhagic tendencies, appears to be the major cause of fatalities in hypersensitive individuals. Best and Paul [4b] concluded that hypoplasia may develop in from two weeks to 13 mo., with an average interval of five months, after the beginning of therapy. This conforms with our experience in the above-reported case, since the patient had been under treatment for a period of five months.

Before treatment is instituted, it is important that hematological studies be performed and that these studies be repeated at monthly intervals.[7] In patients with a history of hypersensitivity to drugs, more frequent blood determinations are advisable. Any diminution of white blood cells (especially of granulocytes), red blood cells or platelets should be interpreted as danger signals warranting discontinuance of therapy. Patients should be advised to report untoward reactions promptly to their physician.

SUMMARY

A fatal case of aplasia of the bone marrow directly attributed to mesantoin® (3-methyl-5,5-phenylethylhydantoin) is presented. The toxic effects of the drug are reviewed and prophylactic hematological studies are suggested.

Newark City Hospital, 116 Fairmount Ave.

5. David, N. A.; Durkin, L. S.; Margason, M. L., and Viele, W. A.: Methyl Hydantoin (Mesantoin) in Treatment of Epilepsy, J. Nerv. & Ment. Dis. **108**: 118 (Aug.) 1948.

6. Ruskin, D. B.: Fulminating Dermatitis Bullosa Medicamentosa Due to "Mesantoin," J. A. M. A. **137**: 1031-1034 (July 17) 1948.

7. Bloom, Lynch, and Brick.[3b] Best and Paul.[4c] Bailey, A. A., and Worden, R. E.: Treatment of Adults for Epilepsy: I. Toxic Effects of 3-Methyl 5-5-Phenylethylhydantoin, Proc. Staff Meet., Mayo Clin. **24**: 483-486 (Sept. 14) 1949.

Renal Tumors.—One can never state that the patient is cured following removal of a malignant renal tumor no matter how localized or favorable the condition may appear at surgery. Conversely, the situation is not entirely hopeless even with renal vein involvement and long duration of the symptoms. The relatives can be told to expect that the patient has somewhat less than a 50 per cent chance of surviving five years after removal of a renal cell carcinoma, but only about half that if the malignant neoplasm arose from the renal pelvis. This, of course, assumes that all gross neoplastic tissue is removed.—Vernon S. Dick, M.D., and Lloyd D. Flint, M.D., The Prognosis of Renal Tumors, *Surgical Clinics of North America*, June, 1951.

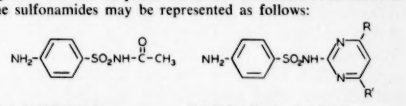
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Acet-Dia-Mer-Sulfonamides.—Tricombisul (Schering).—$C_8H_{10}N_5O_2S$, $C_{12}H_{10}N_4O_2S$ and $C_{11}H_{12}N_4O_2S$.—M.W. 214.24, 250.27 and 264.30.—A sulfonamide mixture containing equal weights of sulfacetamide, sulfadiazine-U.S.P. and sulfamerazine-U.S.P., to which there may or may not be added a suitable compatible agent to increase the pH of the urine. The structural formulas of the sulfonamides may be represented as follows:



SULFACETAMIDE

SULFADIAZINE, R = R' = H
SULFAMERAZINE, R = H, R' = CH_3

Actions and Uses.—See the general statement on Sulfonamide Mixtures (New and Nonofficial Remedies 1951).

For specific indications and contraindications to the use of the drugs, see the general statement on Sulfonamides.

Dosage.—The mixture of acet-dia-mer-sulfonamides is administered orally. In adults, 4 gm. total sulfonamides is given as the initial dose, followed by 1 gm. every four hours until signs of infection have been absent for at least 48 hours. Then 3 to 4 gm. in divided doses is given daily for an additional two to three days depending upon the type and severity of infection. In children, the average daily dose should be calculated on the basis of 0.1 gm. per kilogram of body weight; one-third of this amount is given as the initial dose, followed by one-sixth of the total daily dose every four hours. This amount should be continued as a maintenance dose until signs of infection have subsided for at least 36 hours. Thereafter, two-thirds to one-half of the original maintenance dose may be given for an additional two to three days, again depending upon the type and severity of the infection. The blood concentration of sulfonamides should be maintained between 5 and 15 mg. per 100 cc.

Tests and Standards.—

For description and standards see the U. S. Pharmacopeia under Sulfadiazine, Sulfadiazine Tablets, Sulfamerazine and Sulfamerazine Tablets. For tests and standards on Sulfacetamide-N.N.R., see the monograph for this material.

Dosage Forms of Acet-Dia-Mer-Sulfonamides

TABLETS. *Assay:* (Total Sulfonamides) Accurately weigh at least 20 tablets and grind them. Weigh out an amount of powder equivalent to 0.5 gm. of total sulfonamides. Transfer the powder to a 250 ml. beaker, add 100 ml. of water and 20 ml. of hydrochloric acid, heat on a steam bath until most of the turbidity has disappeared, and cool. Proceed as directed in the assay for sulfadiazine, *U. S. P. XIV*, p. 578, starting with, "... cool to 15° ..." Each milliliter of 0.1 M sodium nitrite is equivalent to 0.02410 gm. of total sulfonamides. The amount of total sulfonamides present is not less than 95.0 nor more than 105.0% of the labeled amount.

Tablets Tricombisul: 0.5 gm. Each tablet contains 0.166 gm. each of sulfacetamide, sulfadiazine and sulfamerazine. Schering Corporation, Bloomfield, N. J.

Aminophylline-U.S.P. (See New and Nonofficial Remedies 1951, p. 297).

Enteric Coated Tablets Aminophylline: 0.1 gm. and 0.2 gm. Boyle & Company, Los Angeles, Calif.

Tablets Aminophylline: 0.1 gm. and 0.2 gm. Boyle & Company, Los Angeles, Calif.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. . . . . CHICAGO 10, ILL.
Edited by . . . . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

INSTRUCTIONS FOR PATIENTS

One of the commonest complaints voiced by patients concerns failure of their physicians to provide adequate instructions to follow after they leave the offices of the physicians. These patients complain that sometimes they think they must be clairvoyant to do what their doctors expect of them. Even those who seem to expect only general directions often mildly voice a suggestion that the medical profession be more explicit when instructions are given to someone who is ill or to his relatives. If prescriptions for drugs can be written in detail so can other instructions, say these critics.

The more commonly heard complaints concern failure to outline in detail diets for those who are required to lose weight, are restricted in their use of food because of lesions in the gastrointestinal tract, or are suffering from hypertension. The average patient will ask how he can lose weight if he does not know the composition of foods, how much he should have, and where he can obtain detailed information. Of equal importance are the vague directions often given to patients who need special shoes or body supports, and to patients who must undergo a series of radiological examinations or laboratory tests. Irritation is certain to arise if these patients find that special shoes are not available in every shoe store or cannot be used by all sufferers regardless of their problems. And the patient who immediately makes his way to a radiological laboratory, after being told to have an "x-ray of the stomach," only to find that he must prepare himself properly for such examination cannot be expected to comment favorably on the interest shown by his doctor or on the intelligence of the medical profession.

Physicians who take the trouble to write or print special instructions or who are specific in their descriptions of shoes and other special items normally are praised for their efforts and become the better liked and less critized members of the profession. They are the ones most frequently remembered by patients asked to recommend doctors to friends. Also well remembered and liked are those who explain the probable outcome when medical or surgical treatment is undertaken and who do not brush aside such inquiries with a brusque "why bother—that's my problem" attitude.

Perhaps such acts may seem like little things, but it is the little things that often mean the difference between success and failure. For their own good, physicians—and their office associates—should always remember the value of these little things. In addition, however, such thoughtfulness brings credit to the medical profession, a consideration of no small significance at any time but which is especially important when some small but vocal group raises cries of selfish interests. The medical profession is as much interested as ever in the patients' welfare, but sometimes this may not be readily apparent to all. Any act that convinces people that the patients' comfort and health still are always uppermost in the thoughts of physicians will do much to offset the statements of those who wish to pervert the thinking of persons receiving medical care.

THE SECOND INTERNATIONAL POLIOMYELITIS CONFERENCE

The Second Poliomyelitis Conference of the International Poliomyelitis Congress, which was held recently in Copenhagen, Denmark, was attended by almost a thousand persons, including almost 600 physicians. Thirty-seven countries were represented, and, if one can judge from the enthusiasm shown by the delegates, as many if not more countries will be heard from when the next conference is called. The information that was exchanged was made available and was received with a degree of understanding that left no doubt concerning its value for those interested in anterior poliomyelitis.

There was no announcement of a miracle drug as a cure or of the development of measures which at this time will prevent this disease in humans, but there was revealed research that shows promise of therapeutic and preventive measures that will permit eventually as much control over this disease as has been attained for other infectious processes. For example, one researcher described experiments that may point the way to the development of a drug that will conquer poliomyelitis by preventing the growth of the virus in the cells of the central nervous system. Experiments conducted in the United States and Australia have already produced methods of inhibiting growth of five different viruses in living cells by chemical attack. An interesting aspect of this report was the failure of these substances to inactivate the virus in test tubes, although in the living cell inactivation could be effected. Another researcher reported on the use of relatively harmless strains of poliomyelitis virus grown in test tubes as vaccines to immunize mice against the disease. Hope was expressed that these experiments might lead to similar developments for humans.

Laboratory procedures, surgery, physical medicine, and other phases of medicine were mentioned for their usefulness as laboratory investigators and practitioners pooled their information. In spite of the years that this disease has been known, poliomyelitis has many confusing aspects and there remains much to be done in the diagnostic, treatment, and corrective fields. While one investigator told of a complement-fixation test that may have clinical application when more is learned about it, another pointed out that a simple diagnostic test is one of the most pressing needs in the fight against poliomye-

V 14
1951

litis. There may be arguments concerning the structure of the cause of this affliction, but there is no doubt that none of the ordinary clinical laboratory examinations provide sufficient data to permit accurate differentiation on the basis of such tests alone. As one investigator reported, the laboratory diagnosis remains a cumbersome, expensive, and highly technical procedure, except, of course, for the fatal case in which the spinal cord becomes available for autopsy. One step in identifying nonparalytic poliomyelitis is to rule out diseases that may present similar symptoms, for example, lymphocytic choriomeningitis, mumps, encephalomyelitis, herpes, infection with a virus of the Coxsackie group, and leptospirosis, but such procedures do not permit the immediate and specific diagnostic determination that is essential.

Commenting on the errors in diagnosis, a clinician warned of other diseases that may be confused with poliomyelitis at some stage in their development. Reporting on experience observed in one hospital, he revealed that of 509 sent to the hospital with a diagnosis of poliomyelitis the diagnosis was shown to be wrong in 71 instances. Included in the 71 were patients with acute arthritis, osteomyelitis, rheumatism, pneumonia, syphilis of the bones, hernia, acute meningitis, chorea, and various inflammatory conditions involving the muscles and nerves. To aid in the avoidance of mistakes, he proposed looking for several traits common to all patients with poliomyelitis: sudden onset in a healthy child; preparalytic initial feverish phase of variable length; frequent occurrence of pain, especially in the back, a short interval before paralysis; severity of paralysis; early appearance and severity of vasomotor disturbances; changes in reflexes; changes in electrical reactions; and changes in the spinal fluid. Also of practical importance were the references by speakers to the relation between activity and severe paralysis, the relation between paralysis and injections of certain immunizing agents and the emotional aftereffects that may be more harmful than the physical handicaps left by the disease. Most patients suffer from shock and fear of loss of life or lasting paralysis, and if they have difficulty in breathing their fears may be intensified. Of no less importance is the need for physical medicine.

The Second International Poliomyelitis Conference was held in a city of beauty, and its people will always be remembered by the members of the Conference for their friendliness. The setting seemed appropriate for consideration of a disease with the emotional appeal of poliomyelitis. Those responsible for the meeting can rest assured of a successful one. The conference was held jointly with the National Foundation for Infantile Paralysis, U. S. A., and the Danish National Association for infantile Paralysis under the auspices of the International Poliomyelitis Congress. Such meetings cannot be prepared for in just a few weeks; months, even years, of planning are necessary when visitors from over the world are to attend and when scientists from many countries are to participate. Once they are assembled, however, the results of such planning prove the need and usefulness of such free exchange of information under circumstances that promote harmony and understanding and are free of suspicion. If more such meetings were held, science might be able to open some doors closed even to diplomats.

JOINT COMMISSION FOR THE ACCREDITATION OF HOSPITALS

At its annual meeting in September, the House of Delegates of the American Hospital Association approved the plan to establish a Joint Commission for the Accreditation of Hospitals. The American Medical Association, the American College of Physicians, and the American College of Surgeons, having agreed to the proposal in earlier meetings, the commission will now be set up with the support and cooperation of the four organizations. The establishment of the Joint Commission will mark the culmination of a year of negotiation, during which the Commission encountered discouraging problems. That the plan has become a reality is a testimonial to those men representing the medical profession and the field of hospital administration who sat through long hours of discussion and debate to reach agreement on points that had seemed to be irreconcilable.

The commission will be the final authority for the accreditation of hospitals, carrying out the standardization program previously sponsored by the American College of Surgeons. The functions of the Commission will be to formulate standards relating to hospital accreditation, to establish the type and scope of inspections to be made under this program, to assign responsibility for hospital inspections to the several participating organizations, and to award certificates of accreditation to qualifying hospitals. Inspections for purposes of hospital accreditation will be made and reported in a uniform manner by staff representatives of the participating organizations, with the reports to be evaluated and acted on by the Commission itself. Inspections will relate primarily to the professional and administrative aspects of the hospital. They will not be concerned directly with the hospital's teaching program. Hospital surveys relating to internship and residency training will continue to be carried out by the organizations that have conducted these programs in the past.

The Joint Commission will be composed of 18 members: six appointed by the American Medical Association, six by the American Hospital Association, three by the American College of Physicians, and three by the American College of Surgeons. A minor change in this representation will be made if the Canadian Medical Association accepts an invitation to participate. In this event it will appoint one representative and the American Hospital Association will appoint an additional member from the Canadian hospitals. The operating expenses of the Commission will be paid by the constituent organization on a basis proportionate to their representation on the Commission. The budget for the first year of operation has been tentatively set at

147
51

$70,000. This amount does not include the costs of hospital inspection service, which will be the responsibility of the individual organizations.

While much work remains to be done before the Commission is in actual operation, the success of the project now seems assured. Agreement on a cooperative basis for carrying out this important program marks a milestone in the history of the relations between these four organizations. It gives confirmation to the belief that though the views of the several groups may at times appear to be in conflict, differences of opinion can be settled if the ultimate objective, that of better patient care, is kept in mind. This cooperative effort refutes those who claim that problems confronting the profession and hospitals today can be resolved only by the intervention of an outside agency. In the same spirit of mutual help, the profession and hospitals can and will move forward in a concerted effort to provide an even better product of physician-hospital care for the final arbiter of its worth, the public.

MEETING OF MILITARY SURGEONS

Last week the Association of Military Surgeons of the United States returned to Chicago, their birthplace, for their 58th annual convention. Last year the meeting was held in New York, next year it will be in New Orleans. The Chicago meeting was well organized and well attended. The scientific program brought before the assembly the Surgeon Generals or their representatives, the chief medical officer of the Veterans Administration, officers recently returned from Korea, and a number of authoritative speakers from civilian life. Emphasis was placed on the outstanding and, in some ways, unprecedented record of medical achievement in the difficult Korean situation. The Commander-in-Chief of the Far East Command, General Ridgway, briefly summed up this achievement in a letter to the Surgeon General of the Army, in which he said, "The death rate in our hospitals is by far the lowest ever known in war. Our medical soldiers have gallantly, and at the risk of their own lives, saved the lives of their armed comrades, being skillfully led by devoted medical officers."

While the Korean records for battle injuries and epidemic diseases have been unusually good, two problems still cause much concern. These are the problem of cold injuries at the front and malaria. Cold injuries receive special attention at all stages of medical service, and centers for the treatment of these battle injuries have been established at Osaka in Japan and at Percy Jones Army Hospital in the United States. The result of the plan of treatment of these casualties has been an extremely low percentage of amputations and, according to Surgeon General of the Army Major General George E. Armstrong, an extremely high percentage of returns to duty.

The incidence of malaria in the fighting forces in Korea has been and remains low. During the first year of the Korean fighting, it was about one-fifth that of the Mediterranean theater and the Philippine Islands during World War II and one-seventh that reported in the Southwest Pacific during the same period. The improved treatment in use guarantees a patient a minimum of illness and discomfort. While an improved suppressant is available, General Armstrong said that no suppressant, no matter how effective, will prevent the eventual appearance of acute malaria. Thus, with more and more Korean veterans returning to the United States, malaria has appeared among them to the extent, he said, of 6,500 cases admitted to medical installations in the United States since the beginning of the year. A great majority of these patients responded rapidly to an average treatment period of seven days. There is little likelihood, General Armstrong believes, in view of precautions taken by the various public health agencies and by the military services, that these cases will be any great threat to the health of the civilian population.

The scientific exhibits were an interesting feature of the annual meeting. These demonstrations forcibly emphasized the fact that the military services and the Veterans Administration are in the front lines in both clinical and laboratory research and are doing their best to bring to our fighting forces and our veterans the best in medical care.

The Association of Military Surgeons of the United States is a credit to the profession of medicine. It is worthy of support by all professional persons who have or expect to serve their country in a medical capacity, which includes also dentists, veterinarians, nurses, the medical service corps, and the woman's medical specialty corps.

V 14
1951

ADDITIONAL CONTRIBUTIONS TO MEDICAL EDUCATION FUND

Financial support for medical education still is in the news throughout the country. Last week the issue made headlines as it was debated on the floor of the United States Senate. The previous week Pennsylvania's state medical society, through its House of Delegates, approved a voluntary assessment of its membership for medical schools. The latter action has importance for the medical profession, as it indicates another step forward by American physicians who are interested in solving such problems voluntarily. By their action, the physicians of Pennsylvania take their place on the ever-growing list of organizations and individuals dedicated to raising money for the unrestricted use of the nation's 79 medical schools. As Pennsylvania's 12,000 doctors of medicine move to support the American Medical Education Fund, the societies of other states are reported to be making similar plans. Plans are being laid for definite campaigns in many parts of the country. Additional contributors to the Foundation, since July 1, are listed on page 763.

ORGANIZATION SECTION

CONTRIBUTORS TO THE AMERICAN MEDICAL EDUCATION FOUNDATION

Following are the names of all individuals and organizations who contributed to the American Medical Education Foundation between July 1 and Oct. 1, 1951.

PHYSICIANS

CALIFORNIA—(10)
Neil D. Elzey
E. A. Filipello
Curtis M. Galt
P. A. Grigorieff
Carl F. Grunewald
Robert W. Huntington
Eric Lindroth
J. Lafe Ludwig
H. Gordon MacLean
Beverly Simpson

COLORADO—(8)
Maurice Chernyk
Louis S. Faust
William Nelson
William A. H. Rettberg
Kenneth Charles Sawyer
Charley J. Smyth
Clyde E. Stanfield
Arthur R. Woodburne

CONNECTICUT—(3)
Joseph H. Howard
Bernhard A. Rogowski
Daniel P. Samson

FLORIDA—(14)
Leo Batell
William C. Blake
R. Hugh Douglas
Orea A. Ellingson
Sherman B. Forbes
B. Martin M'Closky
Marvin B. Miller
John D. Milton
David R. Murphy Jr.
Richard C. Rodgers
Raul Roque
John P. Rowell
Mason Trupp
Lester L. Zipser

GEORGIA—(1)
J. Dudley King

HAWAII—(1)
Valdemar O. Zialcita

ILLINOIS—(15)
Robert R. Anschuetz
Loyal B. Bagnall
Paul L. Bergstrom
Chester L. Crean
Robert T. Fielding
Edwin S. Hamilton
E. B. Howard
Ernest E. Irons
Dwight J. Ladd
Ralph G. McAllister
John G. Meyer Jr.
Lillian L. Rich
Elbridge W. Telford
Willard O. Thompson
Charles Wm. Young

INDIANA—(4)
George E. Gates
Clifford M. Jones
Hugh A. Kuhn
Harry Plummer Ross

IOWA—(19)
Nathaniel G. Alcock
J. F. Aldrich
Louis B. Amick
Robert S. Bell
George Braunlich
Julia Cole
John P. Darling
R. L. Feightner
Arthur F. Fritchen
Leo C. Kuhn
Lester E. Larson
Frederic G. Loomis
James O. McAllister
Arthur E. Perley
Justus B. Roberts
Ivan T. Schultz
Nelle E. T. Schultz
Howard Wilford Smith
Paul W. Van Metre

KANSAS—(2)
Walter Austin Carr
Condon T. Hagan

MAINE—(2)
Frank B. Bull
Charles H. Jameson

MARYLAND—(9)
Margaret W. Lawrence
Kendrick McCullough
Norman Oliver
R. Rhett Rathbone
Charles G. Spicknall
Merton L. White
Samuel B. Wolfe
Henry Wollenweber
George H. Yeager

MASSACHUSETTS—(6)
Samuel Bachrach
Allen G. Brailey
Lonnie O. Farrar
Herbert T. Leighton
Leonard B. Thompson
Sarah Parker White

MICHIGAN—(2)
L. W. Hull
William J. Stapleton Jr.

MINNESOTA—(7)
Edgar Van Nuys Allen
William F. Braasch
Frank J. Heck
Henry F. Helmholz
M. S. Henderson
Victor Johnson
Frederick Wm. Mayer

MISSISSIPPI—(1)
William S. Pennington

MISSOURI—(3)
Leland B. Alford
Robert M. Smith
Charles E. Virden

NEBRASKA—(3)
Walter Benthack
Edwin Davis
C. F. Ferciot

NEW JERSEY—(4)
Willis B. Day
Peter G. Hunziker
Willard H. Lemmerz
A. B. Shapiro

NEW MEXICO—(1)
Benjamin Barzune

NEW YORK—(13)
W. P. Anderton
Louis H. Bauer
Abraham Block
John M. Galbraith
W. B. Hamby
Ralph Charles Kahle
Moses H. Krakow
Paul Mehlman
Capt. Warren C. Miller
M. Murray Peshkin
Harry D. Sewell
Capt. E. J. Tomsovic
H. G. Weiskotten

NORTH CAROLINA—(1)
Eben Alexander Jr.

NORTH DAKOTA—(1)
C. J. Meredith

OHIO—(6)
Charles Spencer Higley
William J. Horger
William Francis Mitchell
Charles M. Oxley
Martyn C. Raupple
Charles F. Shook

OREGON—(2)
Herman A. Dickel
Leonard Allan Gay

PENNSYLVANIA—(13)
S. A. Donghia
Harry S. Good
J. S. Herkness
Louis W. Jones
Louis F. Kirchner
Scott Barr Lewis
William Lee Malley
J. S. Oehrle
Joseph P. Reath
Charles L. Shafer
Morris W. Stroud, III
Joseph B. Vander Veer
James R. Weddell

SOUTH CAROLINA—(2)
Hugh P. Smith Jr.
William Weston

SOUTH DAKOTA—(1)
Roy E. Jernstrom

TEXAS—(3)
Marie Elizabeth F. Gentry
Lt. M. C. Geo. A. Rogers
William E. Watt

UTAH—(1)
Frank K. Bartlett

VIRGINIA—(3)
Wm. C. Salley
Girard V. Thompson
Charles W. Warren

WASHINGTON—(11)
John J. Bonica
I. A. Drues
Robert Wm. Florence
B. D. Harrington
James W. Haviland
William H. Ludwig
George A. Race
Chris C. Reynolds
Duncan Robertson
Charles G. Trimble
James L. Vadheim

WEST VIRGINIA—(3)
Henry Aldis
Robert C. Lawson
Karl J. Myers

WISCONSIN—(7)
Robert Wm. Byrne
Jacob M. Fine
Stephen E. Gavin
Maurice A. Hardgrove
S. A. Morton
Albert Popp
Chester Wade

WYOMING—(1)
J. Cedric Jones

ORGANIZATIONS

Ashland County (Ohio) Medical Society
Fine-Lando Clinic (Wisconsin)
Idaho State Medical Association
Mason Smith Neurological Clinic (Florida)
Red River Valley (Minnesota) Medical Society
Rohlf Memorial Clinic (Iowa)
Woman's Auxiliary to the Colorado State Medical Society

LAY CONTRIBUTORS

Eugene F. Costantino, Tampa, Fla.
Capt. John Albert Goodpasture Jr., Bristol, Va.
Madeline Rue Smith, R.N., Woodward, Iowa
Frances C. Zimmer, Monmouth, Ill.

TOTAL CONTRIBUTORS TO DATE

ALABAMA (15)	NEBRASKA (3)
ALASKA (0)	NEVADA (1)
ARIZONA (0)	NEW HAMPSHIRE (0)
ARKANSAS (3)	NEW JERSEY (8)
CALIFORNIA (38)	NEW MEXICO (10)
COLORADO (87)	NEW YORK (68)
CONNECTICUT (11)	NORTH CAROLINA (5)
DELAWARE (1)	NORTH DAKOTA (1)
DISTRICT OF COLUMBIA (1)	OHIO (57)
FLORIDA (18)	OKLAHOMA (3)
GEORGIA (5)	OREGON (8)
HAWAII (2)	PENNSYLVANIA (51)
IDAHO (0)	PUERTO RICO (1)
ILLINOIS (54)	RHODE ISLAND (0)
INDIANA (14)	SOUTH CAROLINA (9)
IOWA (89)	SOUTH DAKOTA (4)
KANSAS (8)	TENNESSEE (2)
KENTUCKY (4)	TEXAS (16)
LOUISIANA (2)	UTAH (2)
MAINE (3)	VERMONT (0)
MARYLAND (14)	VIRGINIA (9)
MASSACHUSETTS (26)	WASHINGTON (20)
MICHIGAN (16)	WEST VIRGINIA (9)
MINNESOTA (19)	WISCONSIN (9)
MISSISSIPPI (1)	WYOMING (1)
MISSOURI (8)	ORGANIZATIONS (22)
MONTANA (3)	LAY CONTRIBUTORS (12)

MEDICAL NEWS

CALIFORNIA

Stockton Study Club Lectures.—The 13th annual fall series of postgraduate lectures for the Stockton Postgraduate Study Club is being given in the Occupational Therapy Building of the Stockton State Hospital, except for the Nov. 29 dinner meeting, which will be held at Marraccini's Inn. Remaining lectures are as follows:

Oct. 25, Arteriosclerosis: Newer Concepts of Genesis and Treatment, John Gofman, Berkeley.
Nov. 6, Surgical Treatment of Congenital and Acquired Cardiovascular Disorders, Alfred Blalock, Baltimore.
Nov. 8, Treatment of Extensive Burns and Injuries from Explosions, Lewis F. Ellmore, Los Angeles.
Nov. 15, Mitral Stenosis: Diagnosis and Surgical Treatment, Herbert N. Hultgren, San Francisco.
Nov. 29, Common Behavior Problems in Children, Hale F. Shirley, San Francisco.

University Promotions.—Fifty-one members of the faculty of the University of California School of Medicine, San Francisco, have received academic advancements. Among them are Dr. Bertram V. A. Low-Beer, who has been advanced to professor of radiology, and Dr. Alexander Simon, advanced to professor of psychiatry. Four were promoted to clinical professorships: Dr. Thomas Floyd Bell, obstetrics and gynecology; Dr. Michael J. Hogan, ophthalmology; Dr. Mary B. Olney, pediatrics; and Dr. Robert Wartenberg, neurology.

COLORADO

Harvard Lecture.—The fourth annual Harvard Lecture will be delivered by Dr. William B. Castle, director of the Thorndike Memorial Laboratory and professor of medicine at the Harvard Medical School, Boston, on Nov. 9 in the Denison Auditorium of the University of Colorado Medical Center, Denver. Dr. Castle will speak at 5 p. m. on red cell destruction in hemolytic anemias. Physicians, medical students, nurses, and other interested persons are cordially invited to attend. The lecture is being arranged by the Rocky Mountain Harvard Medical School Alumni Association.

Heart Research Center.—Construction of a modern heart research center in the Rocky Mountain area is underway at the University of Colorado School of Medicine, Denver. The laboratories, being built as the third floor over the present two-story Verner Z. Reed Outpatient Clinics at the Medical Center, are expected to be completed by January, 1952. The project is being financed by a grant of $250,000 from the National Heart Institute of the U. S. Public Health Service. Although called a "heart center," research on cardiovascular-pulmonary diseases, which include all types of heart and blood vessel diseases as well as lung-heart ailments, will be conducted there. Research in blood diseases will also be undertaken. The center will consist of 42 rooms.

FLORIDA

City Honors Veteran Physician.—Citizens of Palmetto honored Dr. John O. Brown, their physician for 57 years, at an outing in the local park on the occasion of his 87th birthday. Civic organizations took charge of the celebration, and the doctor received several gifts. Although Dr. Brown stopped calling on patients several years ago, many people still go to his home for consultation.

GEORGIA

Personal.—Dr. Morris Schaeffer, former consultant at the Veterans Administration Hospital in Montgomery, has joined the faculty of Emory University School of Medicine, Atlanta, as an associate professor of bacteriology and immunology,

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Medical Press Conference.—"The Editor and His Responsibility to the Community for the Improvement of Medical Service" will be the theme of the second annual Medical Press and Radio Conference of the Medical Association of Georgia to be held Oct. 26 at the Dempsey Hotel, Macon. Among the speakers will be Mr. Leo Brown, Public Relations Director, American Medical Association, Chicago, and Dean Raymond B. Nixon, Emory University School of Journalism, Atlanta.

ILLINOIS

Personal.—Dr. Harold E. Himwich, chief, clinical research division, Chemical Corps Medical Laboratories, Army Chemical Center in Maryland, has been appointed director of the research division of the Cottage Hospital at Galesburg.

Dr. Keeton Retires as Department Head.—Dr. Robert W. Keeton, who recently retired after 18 years as head of the department of internal medicine at the University of Illinois, was honored Oct. 4 at a dinner attended by over 400 persons. A "Festschrift" was presented to Dr. Keeton. The commemorative volume consists of 36 original scientific papers written by his colleagues, former students, and friends. Dr. Keeton has been associated with the university continuously since 1925. Prior to that time he taught at Albany (N. Y.) Medical College.

Chicago

Personal.—Dr. Ulysses G. Dailey left New York Oct. 7 for Pakistan, where he will give lectures and clinics in surgery at the three medical centers of that country, Karachi, Lahore, and Dacca. The assignment under an exchange agreement between the State Department of the United States and the Pakistani government began Oct. 15. Dr. Dailey plans to return to his practice about Feb. 1, 1952.

Blood Donor Center.—The first Red Cross defense blood donor center in Chicago since World War II opened Sept. 8 at 116 S. Michigan Ave. Up to this time nine hospitals and three mobile units have handled blood donations. The Defense Department requested a step-up of processing. The new center, equipped with 16 beds, can handle 275 donations a day. The Chicago goal for the year is 173,000 pints; the national goal is 5 million pints.

Dr. Kretschmer Leaves Fund for Research.—Northwestern University will receive approximately one million dollars from the estate of Dr. Herman L. Kretschmer, Chicago urologist, who died Sept. 23 (THE JOURNAL, Sept. 29, p. 522). Dr. Kretschmer's will specified that the money should be used to establish the "Lucy and Edwin Kretschmer Fund of Northwestern University Medical School" for "special studies and investigations in the field of urology." The fund will be a memorial to his first wife, who died in 1942, and to his son who died in 1941 at the age of 15. According to the terms of the will, Northwestern University is made the residuary beneficiary of his estate, the amount ultimately accruing to the university being conservatively estimated as in excess of $500,000. In addition, the university will receive about $275,000 from Dr. Kretschmer's life insurance, and the remainder, after a life estate to Dr. Kretschmer's wife, Mrs. Marion Ellen Kretschmer, in a trust fund now valued at about $18,000.

IOWA

County Society Centennial.—The Polk County Medical Society will observe its centennial Oct. 24 beginning with a luncheon at the Hotel Sargent in Des Moines. Speakers at the afternoon and evening sessions will be the following:

Carl A. Moyer, Dallas, Texas, This Is an Acute Abdomen.
Carl V. Moore, St. Louis, Advances in Our Knowledge of the Anemias.
Walter L. Bierring, Des Moines, Medical Pioneers of Polk County.
George F. Lull, Chicago, Secretary and General Manager, American Medical Association, Progress in Medicine (Tentative).

V 14
1951

Conference on Children.—Governor Beardsley has called a conference of all persons who are working with children to review the surveys made by the committee of the Iowa Commission on Children and Youth last year in preparation for the Mid-century White House Conference. Dr. Henry F. Helmholz, Rochester, Minn., will speak following a dinner at East High School at 6 p. m.

KANSAS

Course in Gynecologic Cancer.—A course in the diagnosis and treatment of gynecologic cancer will be given Nov. 12-14 at the University of Kansas Medical Center, Kansas City, by the university in cooperation with the Kansas Medical Society and the state board of health. Enrollment is open to any doctor of medicine. The course is planned for both the specialist and the doctor in general practice. Interns and residents, on identification by their hospital superintendents, will receive complimentary enrollment. Guest instructors will be Dr. Ludwig A. Emge, clinical professor emeritus of obstetrics and gynecology, Stanford University School of Medicine, San Francisco; Dr. Norman F. Miller, professor of obstetrics and gynecology, University of Michigan, Ann Arbor, and Dr. Janet T. Towne, assistant clinical professor of obstetrics and gynecology, Stritch School of Medicine, Loyola University, Chicago. In addition, members of the University of Kansas faculty will serve as instructors. Advance registration is requested, and may be made by writing to the Medical Center, Kansas City 12.

MASSACHUSETTS

Course in Electrocardiography.—This full-time course will be given Nov. 5-9 under the auspices of the Beth Israel Hospital, Boston, Postgraduate School. The title will be "Practical Electrocardiographic Interpretation." The fee will be $50. The course is designed for practicing physicians who desire a short but practical introduction to the use of electrocardiograms in general practice.

Anesthesia Teaching Program.—A program for teaching anesthesiology has been initiated as a cooperative effort of the departments of anesthesia of several hospitals in Boston. Sessions are held each Monday evening at the Stearns Auditorium of the New England Medical Center, 25 Bennet St., 7-9 p. m. All physicians are invited. Hospitals participating are Boston City, Boston Lying-In, Children's Medical Center, Massachusetts Memorial, New England Deaconess, New England Medical Center, and Peter Bent Brigham.

Dunham Lectures.—Dr. E. B. Verney, professor of pharmacology, University of Cambridge, England, will deliver the Edward K. Dunham Lectures for the Promotion of the Medical Sciences at Harvard Medical School, Boston, Oct. 30, Nov. 1, and Nov. 6 at 5 p. m. The general subject of the lectures is the excretion of water by the kidney, with special reference to its neurohypophysial control. The first lecture will be on "Glomerular Function and the Fate of the Filtrate Water," and succeeding lectures on "The Specific Excretion of Water and the Factors Which Affect It," and "The Osmotic Control of the Release of the Antidiuretic Hormone." Interested professional persons are invited.

MICHIGAN

State Society Cites General Motors.—The Michigan State Medical Society has presented three scrolls to General Motors Corporation for its work in industrial medicine. The presentations stemmed in part from the corporation's grant of $1,500,000 last December for establishment of the Institute of Industrial Health at the University of Michigan, Ann Arbor. Those to whom scrolls were presented are Charles E. Wilson, corporation president; Dr. Max R. Burnell, medical director, and Dr. Clarence D. Selby, retired medical consultant. Presentations were made at a luncheon at the General Motors Building, Detroit.

Annual Cancer Meeting in Detroit.—The Detroit Institute of Cancer Research will hold its fourth annual scientific meeting Oct. 22-24 in the auditorium of the Engineering Society of Detroit, Horace H. Rackham Educational Memorial. There will be no fee for registration. The following program will be presented:

Charles H. Best, Toronto, Canada, Factors Which Control the Fat Content of Liver Cells.
James A. Miller, Ph.D., Madison, Wis., Biochemical Aspects of Experimental Hepatic Carcinogenesis.
Michael Heidelberger, Ph.D., New York, Quantitative Immunochemical Studies on the Purified Mild Factor Causing Mammary Carcinoma in Mice.
Milan J. Kopac, Ph.D., New York, Microrgical Studies on Living Cells.
Keith R. Porter, Ph.D., New York, Observations on the Fine Structure of Protoplasm.
Erwin Chargaff, Ph.D., New York, Studies on the Composition and Properties of Nucleic Acids.
Vincent du Vigneaud, Ph.D., New York, Transmethylation and Biological Syntheses of Labile Methyl Groups.
Hans Neurath, Ph.D., Seattle, Chemical Behavior and Mode of Action of Proteolytic Enzymes.
Hans Selye, Montreal, Canada, The General Adaptation Syndrome and Tumor Regenesis.

The last four speakers are sponsored by the American Cancer Society, Southeastern Michigan Division, as a part of its professional education program.

Alton Ochsner, New Orleans, Prospects for Diagnosis and Cure of Bronchiogenic Carcinoma.
James Barrett Brown, St. Louis, Neck Dissection for Metastatic Carcinoma.
Ira T. Nathanson, Boston, Endocrine Substances as Chemotherapeutic Agents in the Management of Advanced Cancer.
Cushman D. Haagensen, New York, Challenge of Mammary Carcinoma.

MINNESOTA

Rigler Lecture.—Dr. W. Edward Chamberlain, professor of radiology, Temple University, Philadelphia, will give the annual Leo G. Rigler lecture at the University of Minnesota Medical School, Minneapolis, on Nov. 1. He will speak on recent advances in equipment for fluoroscopy at 8:15 p. m. in the auditorium of the Minnesota Museum of Natural History. Dr. Chamberlain will also participate in a continuation course on roentgenology of chest diseases, which will be presented at the Center for Continuation Study from Oct. 29 to Nov. 3. The lectureship was established in 1944 by colleagues, friends, and former students of Dr. Rigler in recognition of his contributions in teaching and research in radiology. He has served as professor of radiology since 1929 and as chairman of the department of radiology at the university since 1937.

MISSOURI

Graduate Medical Course.—The University of Kansas School of Medicine, Kansas City, Kans., in cooperation with the Missouri Academy of General Practice is presenting a postgraduate medical course at Burge Hospital in Springfield beginning Oct. 16 and running through April 15, at afternoon and evening sessions starting at 3 p. m. Dates of lectures are Oct. 16, Nov. 13, Dec. 18, Jan. 15, Feb. 19, and April 15. A registration fee of $25 is required to cover the cost of the course, although parts of the sessions may be attended at a fee of $5 for each program.

NEBRASKA

Dr. Gillick Named Dean at Creighton.—Dr. Frederick G. Gillick has been appointed dean of Creighton University School of Medicine, Omaha, succeeding Dr. Percy J. Carroll. Dr. Gillick served on the staffs of the St. Louis University's St. Mary's Group of Hospitals. He became instructor in internal medicine at the university in 1940 and left to become a research assistant in medicine at the University of California, San Francisco, in 1946. When he left there in 1949 he joined the U. S. Public Health Service.

NEW YORK

General Practice Assembly.—The second annual scientific assembly of the American Academy of General Practice, Nassau County Chapter, will be held Nov. 14 at the Garden City Hotel in Garden City. Speakers will include the following:

H. Flanders Dunbar, New York, Personalities of Potential Centenarians.
Henry Bockus, Philadelphia, Peptic Ulcer.
Hans Selye, Montreal, Canada, Stress and the Adaptation Syndrome.
Philip Thorek, Chicago, Jaundice.

Bone Bank in Utica.—One of the first bone banks in the area was established recently at St. Luke's Home and Hospital, Utica, through a gift from an anonymous donor. Bone stored in the bank will be available to surgeons throughout the area. Dr. John F. Rudolph, who was in charge of the bone bank at the Cleveland Clinic before entering practice in Utica, will take charge of St. Luke's bank. Storage will be limited to six months.

New York City

Second Harvey Lecture.—Dr. Frank R. Winton, professor of pharmacology, University College, London, England, will deliver the second Harvey Lecture of the current series at the New York Academy of Medicine Oct. 25 on "Hydrostatic Pressures Affecting the Flow of Urine and Blood in the Kidney."

Fellowship in Medicine.—Applications are being received for a two-year fellowship in medicine at Cornell-New York Hospital to work with Drs. Harold G. Wolff, William H. Dunn, and Stewart Wolf. One-half time will be spent in experimental work and one-half in clinical experience with patients with stress disorders. The fellowship is to begin in July, 1952.

Complete Cancer Unit.—The new Tower Building of the Memorial Center for Cancer and Allied Diseases was dedicated Sept. 25. The six-story structure increases the capacity for outpatient treatments from 100,000 to 250,000 persons. Laurance S. Rockefeller, speaker at the ceremonies, said that the dedication marked "a significant milestone in the history of organized attack on disease," since "for the first time in the history of medical practice patients of a city hospital are now treated in a building belonging to a voluntary institution."

OHIO

Lake Hope Tuberculosis Conference.—Members of the Ohio and the American Trudeau societies, specialists in diseases of the chest, and superintendents and staff members of tuberculosis hospitals in Ohio will hold a three-day conference on tuberculosis at Lake Hope Lodge, Zaleski State Park, Nov. 9-11. Purpose of the conference is to raise the standards of handling tuberculosis cases throughout the state. The conference is actually a workshop in the care and treatment applied to a series of consecutive cases from different tuberculosis hospitals. Three tuberculosis hospitals will provide data on a series of 25 consecutive admissions dating from January, 1950. Complete histories, x-rays, treatment, surgery, all procedures used, and the results will be reported to the conference. Each case will then be discussed. Moderators for the three half-day sessions include Dr. Paul T. Chapman, Detroit, tuberculosis controller; Dr. Sidney E. Wolpaw, Cleveland, president, Ohio Trudeau Society, and Dr. John H. Skavlem, Cincinnati, president of the American Trudeau Society. On Saturday night a series of cases of diseases of the chest with proved diagnosis will be presented and discussed by a panel including Dr. H. McLeod Riggens, New York, Dr. Benjamin Felson, Cincinnati, Dr. Chapman, and two members not yet named. The conference is being sponsored by the Ohio Tuberculosis and Health Association. The registration fee is $10.

PENNSYLVANIA

State Medical Election.—Newly elected officers for the Medical Society of the State of Pennsylvania include Dr. Louis W. Jones, Wilkes-Barre, president; Dr. Theodore R. Fetter, Philadelphia, president-elect; and Dr. Walter F. Donaldson, Pittsburgh, secretary-treasurer.

Philadelphia

Appoint Temporary Vice-President of University.—Dr. Isador S. Ravdin has been appointed vice-president of the University of Pennsylvania in charge of medical affairs as temporary successor to Dr. Robin C. Buerki, recently resigned. Dr. Ravdin is John Rhea Barton Professor of Surgery and director of the Harrison Department of Surgical Research at Pennsylvania. While serving as vice-president he will have as his special assistant in that office Dr. John McK. Mitchell, dean of the school of medicine. Both Dr. Ravdin and Dr. Mitchell will continue to serve in their present posts at the university in addition to carrying on their new duties. Dr. Ravdin was named director of the Harrison Department of Surgical Research in 1936 and was appointed to the senior chair in surgery in 1945. Before that he held other faculty posts including the J. William White Professorship of Surgical Research and the Harrison Professorship of Surgery. He also has been assistant surgeon at the University, Graduate, and Philadelphia General hospitals. During the recent war Dr. Ravdin, who attained the rank of brigadier general in the Army, was in command of an Army hospital in India, which was organized at the university.

Dr. Buerki resigned as vice-president in charge of medical affairs to become executive director of the Henry Ford Hospital in Detroit. At a convocation in September Dr. Buerki was awarded the honorary degree of doctor of science. During 7 of his 10 years of service at the university he was dean of the Graduate School of Medicine, director of the Temple University Hospital, and director of Graduate Hospital of the University of Pennsylvania.

TEXAS

Visiting Professor.—Kenneth Franklin, D.M., professor of physiology at the University of London, England, will be guest lecturer in physiology at the University of Texas Medical Branch, Galveston, during the week of Nov. 12. Dr. Franklin is visiting professor of physiology at the University of Illinois, Urbana. He will come to Galveston following a week's visit in New Orleans. After his stay at Galveston Dr. Franklin will visit the Baylor Medical College, Houston, and Southwestern Medical School of the University of Texas at Dallas for lectures in physiology.

Postgraduate Courses.—The first postgraduate session for the current academic year at the University of Texas Medical Branch, Galveston, will be held Oct. 28 to Nov. 1. On Oct. 28 the Guest Lecturers in Radiology at the Medical Branch will present a special program dealing with current advances in radiology. From Oct. 30 to Nov. 1 the Tenth Tumor Postgraduate Course offered by the Medical Branch will be presented in cooperation with the Texas State Medical Association. Visiting speakers will include Dr. Matthew J. Stewart, emeritus professor of pathology, University of Leeds Medical School, England; Dr. John F. Holt, University of Michigan Medical School, Ann Arbor; Dr. John D. Martin Jr., Emory (Ga.) University School of Medicine; Dr. John P. North, Veterans Administration Hospital, McKenney, and Dr. Charles Phillips and Dr. Clyde A. Stevenson, Scott-White Clinic, Temple. The program will deal with tumors of the gastroenteric tract and will be under the direction of the John Sealy Hospital Tumor Clinic.

V 14
1951

VIRGINIA

Hospital Residents Meeting.—The annual meeting of the former residents of the Gill Memorial Eye, Ear and Throat Hospital was held at the hospital Sept. 17. The officers of the association include Dr. F. Buerk Zimmerman, Louisville, Ky., president, and Dr. Houston L. Bell, Roanoke, secretary-treasurer.

McGuire Lecture Series.—The 23rd annual Stuart McGuire Lecture Series and a symposium on cardiac surgery and cardiology will be given Nov. 7-9 in the Egyptian Building of the Medical College of Virginia, Richmond. Dr. Claude S. Beck, professor of neurosurgery at the Western Reserve University School of Medicine, Cleveland, will deliver the lectures, the first at 8:30 p. m. Nov. 7 on "Surgical Approach to Coronary Artery Disease," and the second at a corresponding time Nov. 8 on "Resuscitation." Visiting lecturers on the symposium, which is to run Nov. 8 and 9 from 10 a. m. to 4 p. m., are Drs. Charles P. Bailey, Philadelphia; George E. Burch, New Orleans; Daniel F. Downing, Newark, N. J.; Richard W. Eckstein, Cleveland; Harold Feil, Cleveland; John H. Gibbon Jr., Philadelphia; Donald E. Gregg, Washington, D. C., and Irving S. Wright, New York. There is no charge for the McGuire Lectures. A fee of $5 a day for the symposium lectures will be charged to all except members of the faculty of the Medical College of Virginia, Medical Department of the University of Virginia, physicians of the Veterans Administration Hospital, medical students, and members of the house staff of any hospital. Attendance is limited by the seating capacity of the auditorium.

WISCONSIN

Honor Veteran Physician.—All the people of Clinton, 1,100, and many others turned out Sept. 30 to honor Dr. William O. Thomas, who has practiced in the community for 50 years. Representatives of both the Rock County and the Wisconsin state medical societies took part in the program. The doctor was given a complete outfit of photographic equipment.

Rural Health Conference.—The Committee on Rural Health, in cooperation with 55 state organizations interested in improving the health of farm people, is sponsoring the second annual Wisconsin Rural Health Conference in Stevens Point, Oct. 25-26. Emphasis is being placed on farm and home safety, sanitation, nutrition, mental health, care of the aged, health councils, and health insurance.

Personal.—Dr. Simpson M. Markson, clinical professor and director of the department of dermatology at Marquette University School of Medicine, Milwaukee, retired from teaching duties on Sept. 1, but will continue in private practice. His successor is Dr. Harry R. Foerster Sr. Dr. Foerster, who will also continue in private practice, received the rank of clinical professor on Sept. 1. He is a 1914 graduate of the University of Pennsylvania Medical School and has been on the staff of Marquette University School of Medicine since 1921.

WYOMING

Report of State Medical Meeting.—At the annual meeting of the Wyoming State Medical Society in Rock Springs, Sept. 27-29, Dr. Paul R. Holtz, Lander, was installed as president. Other officers for the year are Dr. Edward J. Guilfoyle, Newcastle, president-elect; Dr. James W. Sampson, Sheridan, vice-president; Dr. Glenn W. Koford, Cheyenne, secretary, and Dr. Peter M. Schunk, Sheridan, treasurer. The house of delegates passed resolutions to revamp the medical practice act, approved a mental health program in the State Health Department, and approved fluoridation of public water supplies.

GENERAL

Clinical Research Society.—The Central Society for Clinical Research will hold its annual meeting at the Drake Hotel, Chicago, Nov. 2-3. A series of 34 papers will be presented by members of the society and invited speakers.

Personal.—Dr. Herman W. Kumm has been appointed assistant director of research for the National Foundation for Infantile Paralysis. He has been a representative of the Rockefeller Foundation in Brazil and other South and Central American countries.

Pan American Women Physicians to Meet.—The Pan American Medical Women's Alliance will hold its third conference in Montevideo, Uruguay, Dec. 2-8. Dr. Elizabeth Mason-Hohl, Los Angeles, is president, and Dr. Maria Delgado de Solis Quiero of Mexico is president-elect. The conference will consider subjects of consequence to women and children of this hemisphere.

Society Elections.—At the annual meeting of the American Society of Maxillofacial Surgeons, Sept. 24 in Chicago, Dr. Reed O. Dingman, Ann Arbor, Mich., was elected president; Dr. Fred S. Dunn, New York, vice-president; Dr. Casper M. Epsteen, Chicago, secretary-treasurer, and Dr. Frank F. Kanthak, Atlanta, Ga., member of the Board of Trustees. The next annual meeting will be held in September, 1952, in San Diego, Calif.

Tropical Medicine Meetings.—The American Society of Tropical Medicine, the National Malaria Society, the American Society of Parasitologists, and the American Academy of Tropical Medicine will hold their meetings conjointly this year at the Congress Hotel, Chicago, Nov. 14-17. Features of the meeting will be two panel discussions, Tropical Medicine in the Armed Forces, and Resistance of Insects to Insecticides and a symposium on "The Ecology of Vectors of Parasitic Diseases."

Forum on Prolonged Illness.—The Research Council for Economic Security will present a forum and luncheon meeting on prolonged illness Oct. 30 in the Congress Hotel, Chicago. The panel, beginning at 10 a. m. under the chairmanship of Leon Werch, director of research for the council, will first take up the problem of prolonged illness, and then the research council's survey on the economic aspects of prolonged nonoccupational illness among employed persons. Admission and luncheon fee is $4.50.

Southern Medical Association.—This association will hold its annual meeting in Dallas, Texas, Nov. 5-8, under the presidency of Dr. Curtice Rosser of Dallas. Headquarters will be at the Adolphus Hotel. At the opening assembly at the Baker Hotel, Humphrey Lee, Ph.D., president of Southern Methodist University, Dallas, will speak on "A Layman Views the Medical Scene." He will be followed by Dr. John W. Cline, San Francisco, President of the American Medical Association, who will give an address on "The Problems Confronting Medicine in the Immediate Future." The scientific program will be presented in 22 section meetings. A program of motion pictures has been planned for Tuesday and Wednesday and will run from 9 a. m. to 5:30 p. m. Both technical and scientific exhibits will be on display. The Auxiliary of the Southern Medical Association will meet at the Baker Hotel in conjunction with the association.

Grants for Scholars in Cancer Research.—A limited number of American Cancer Society Scholars are appointed annually on recommendation of the Committee on Growth of the National Research Council. A grant of $10,000, payable over three years, will be made directly to each Scholar's institution by the American Cancer Society as a contribution toward his support or his research, or both. Medical schools, hospitals, research institutes, and other institutions with a primary or substantial interest in cancer research are invited to submit applications. Applications for grants to be effective July 1, 1952, should be submitted prior to Jan. 1, 1952. Inquiries or requests for application forms should be addressed to the Executive Seecretary, Committee on Growth, National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C.

Inquiry regarding Damon Runyon Clinical Fellowships, formerly recommended by the Committee on Growth, should now be addressed to the Damon Runyon Memorial Fund, Hotel Astor, Broadway and 44th St., New York 19.

Annual Prize Essay Contest.—The American Dermatological Association is again offering a prize of $300 for the best essay submitted for original work, not previously published, relative to some fundamental aspect of dermatology or syphilology. Manuscripts typed in English with double spacing, together with illustrations, charts, and tables, all of which must be in triplicate, are to be submitted not later than Dec. 1 to Dr. Louis A. Brunsting, Secretary, American Dermatological Association, 102-110 Second Ave., Southwest, Rochester, Minn. Manuscripts incomplete in any of the above respects will not be considered. Competition in this prize contest is open to scientists generally, not necessarily to physicians. The essays are judged on the following considerations: (1) originality of ideas; (2) potential importance of the work; (3) experimental methods and use of controls; (4) evaluation of results; (5) clarity of presentation; (6) historical background; and (7) bibliography. This contest is planned as an annual one, but if in any year no paper worthy of a prize is offered, the award may be omitted. The prize-winning candidate may be invited to present his paper before the annual meeting of the American Dermatological Association, April 23-26, 1952, at the Broadmoor, Colorado Springs, Colo.

Gorgas Award.—Rear Admiral Charles S. Stephenson, MC, U.S. Navy, retired, Washington, D. C., has been named the ninth recipient of the Gorgas Medal presented annually by Wyeth, Inc., to a doctor in the armed forces who has distinguished himself by his contribution to military medicine. The presentation was made Oct. 9 during the annual dinner meeting of the Association of Military Surgeons of the United States in Chicago. John D. Cash, vice-president of Wyeth, Inc., presented the silver Gorgas medallion and scroll, accompanied with a $500 cash award. Admiral Stephenson, who was selected by the association, was cited for "distinguished service to our military forces in the field of disease prevention and health conservation." Admiral Stephenson was appointed in 1942 the first director of

the United States of America Typhus Commission and during World War II he contributed to the defense against typhus. The Navy awarded him the Legion of Merit. Admiral Stephenson entered the medical corps of the Navy in 1912 and retired from naval service in 1944.

The Gorgas Award was established by Wyeth, Inc., in 1942 in memory of Surgeon General William Crawford Gorgas, whose work in preventive medicine made possible the construction of the Panama Canal.

Lasker Awards, 1951.—The 1951 winners of the annual Lasker Awards of the American Public Health Association were announced at a press luncheon at the Sherry Netherland Hotel, New York, Oct. 8. This year's citation of three women physicians who have practiced medicine for more than 50 years each is unprecedented, Dr. Ernest L. Stebbins, Baltimore, committee chairman noted. Given for the sixth year, the 1951 Lasker Awards were conferred on the following:

Dr. Florence R. Sabin of Denver, "for outstanding accomplishments in public health administration," as a member of the Colorado Post-war Planning Committee and as manager of health for Denver.

Dr. Elise L'Esperance, founder of the Strang Clinics in New York City, and Dr. Catharine Macfarland, professor at Pennsylvania Women's Medical College, Philadelphia (Joint Award), for their "inspiring application of preventive medicine to cancer control."

Karl F. Meyer, Ph.D., director of the Hooper Foundation at the University of California Medical Center, San Francisco, "for bacteriological research that has benefited mankind for four decades."

Dr. William G. Lennox of Boston's Children's Medical Center, and Dr. Frederic A. Gibbs, professor of neurology at the University of Illinois Medical College, Chicago (Joint Award), "able and effective investigators in epilepsy, whose work has saved a host of sufferers from misery."

Group Awards were conferred on the following:

The Health Insurance Plan of Greater New York, "for courageous pioneering with a combination of group medical practice and prepayment to provide comprehensive health services of high quality."

Alcoholics Anonymous, "in recognition of its unique and highly successful approach to that age-old public health and social problem, alcoholism."

The awards will be formally presented to the winners at the annual meeting of the American Public Health Association in the War Memorial Opera House at San Francisco, Oct. 30.

Recurrence of Yellow Fever.—At the annual meeting of the directing council of the Pan American Sanitary Organization in Washington, D. C., Sept. 24, Dr. Fred L. Soper, director of the Pan American Sanitary Bureau, presented a report covering the health activities and the administration of the bureau in the six-month period ending June 30. He reviewed the recurrence of yellow fever in various tropical and subtropical forested areas of the American continent. He pointed out that very little human yellow fever was reported in 1946, 1947, and 1948, but that in November, 1948, cases did occur east of the Panama Canal, followed by scattered cases in 1949, 1950, and 1951 in Panama, and seemed to be moving in a westerly and northerly direction. This movement, he said, indicated a definite sweep of the disease as illustrated by its recent appearance in Costa Rica. Reminiscent of the spread of the disease in Brazil, Argentina, and Paraguay in 1938-40, Dr. Soper said, is the wave of an epizootic development (the spread of the disease in animals), as cases are today moving toward the border of Nicaragua. "We may anticipate," he said, "a movement to and possibly through Nicaragua, Honduras, Guatemala, and southern Mexico." This brings us to the conclusion, he stated, that Central America and southern Mexico may have to be added to the epizootic area of yellow fever. The only probable exception in Central America, he added, might be El Salvador, where very few monkeys exist. As an illustration of a similar movement of the disease in South America, Dr. Soper said that in a serious outbreak in southern Bolivia in 1950 and in that same year in southwest Brazil, there was registered an epidemic of over 2,000 cases with several hundred deaths. Also in 1951 the first cases since 1915 were found in Ecuador, west of the Andes mountain range. The continuing seriousness of the problems of yellow fever in this hemisphere emphasizes the need for the bureau, in cooperation with public health authorities throughout the continent, to maintain its vigilance in the campaign to eradicate the urban vector of the disease and to extend the programs of vaccination in the jungle areas as the only preventive measure available in such forested areas. There are three laboratories in this hemisphere that are currently producing yellow fever vaccine. They are located in the United States at Hamilton, Mont., and in Bogota, Colombia and Rio de Janeiro, Brazil. The bureau has entered into agreement with the governments of the latter two countries in connection with required vaccine standards and in regard to the supply of vaccine for use in neighboring countries.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States in the weeks ended as indicated:

Area	Oct. 6, 1951	Sept. 29, 1951	Oct. 7, 1950
New England States			
Maine	4	2	8
New Hampshire	1	1	1
Vermont	..	5	1
Massachusetts	14	12	38
Rhode Island	2	..	1
Connecticut	23	20	35
Middle Atlantic States			
New York	72	97	286
New Jersey	20	20	48
Pennsylvania	49	60	106
East North Central States			
Ohio	69	64	157
Indiana	17	34	41
Illinois	87	111	125
Michigan	68	64	150
Wisconsin	102	94	65
West North Central States			
Minnesota	34	28	27
Iowa	17	23	89
Missouri	51	42	14
North Dakota	6	..	3
South Dakota	8	7	5
Nebraska	21	20	17
Kansas	39	40	33
South Atlantic States			
Delaware	..	..	3
Maryland	5	7	51
District of Columbia	3	3	4
Virginia	13	14	55
West Virginia	16	16	28
North Carolina	11	16	31
South Carolina	3	1	16
Georgia	16	29	25
Florida	4	4	14
East South Central States			
Kentucky	17	10	42
Tennessee	31	40	28
Alabama	16	27	12
Mississippi	29	37	9
West South Central States			
Arkansas	9	19	9
Louisiana	27	37	4
Oklahoma	16	19	18
Texas	55	66	64
Mountain States			
Montana	7	15	1
Idaho	1	2	5
Wyoming	13	14	..
Colorado	44	34	12
New Mexico	5	6	4
Arizona	8	3	1
Utah	34	27	5
Nevada	2	2	..
Pacific States			
Washington	18	32	30
Oregon	20	19	23
California	145	162	69
Territories and Possessions			
Alaska	4	2	16
Hawaii	2	..	1
United States	1,278	1,407	1,830

CORRECTIONS

Spinal Anesthesia in Postpartum Atony of the Uterus.—In the medical literature abstract with this title appearing in THE JOURNAL of Sept. 15, 1951, page 281, the concentration of procaine hydrochloride should be 1.0%.

Leptospiral Infection Treated with Terramycin.—In THE JOURNAL, Sept. 8, 1951, page 123, right hand column, line 29, the words "where living organisms" should read "where formalinized organisms." In line 34 in this column the words "with living organisms" should read "with formalinized organisms."

V 14
1951

MEETINGS

AMERICAN MEDICAL ASSOCIATION CLINICAL SESSION, Los Angeles, Dec. 4-7. Dr. George F. Lull. 535 N. Dearborn St., Chicago 10, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Toronto, Canada, Oct. 20-25. Dr. E. H. Christopherson, 636 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA, The Seigniory, Montebello, Quebec, Canada, Oct. 23-25. Dr. Charles G. Johnston, 1512 St. Antoine St., Detroit 26, Secretary.

AMERICAN ASSOCIATION OF BLOOD BANKS, Hotel Nicollet, Minneapolis, Oct. 22-24. Miss Marjorie Saunders, 3301 Junius St., Dallas 1, Texas, Secretary.

AMERICAN CANCER SOCIETY, New York, Oct. 25. Dr. Charles S. Cameron, 47 Beaver St., New York, Medical Director.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, Skytop, Pa., Nov. 5-7. Dr. Marshall N. Fulton, 124 Waterman St., Providence, R. I., Secretary.

AMERICAN COLLEGE OF SURGEONS, Fairmont Hotel, San Francisco, Nov. 5-9. Dr. Michael L. Mason, 40 E. Erie St., Chicago 11, Secretary.

AMERICAN PUBLIC HEALTH ASSOCIATION, Civic Auditorium, San Francisco, Oct. 29-Nov. 2. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Chicago, Nov. 4-5. Dr. O. J. Pollak, Quincy City Hospital, Quincy 69, Mass., Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, Washington, D. C., Nov. 5-8. Dr. J. Earl Remlinger Jr., 188 W. Randolph St., Room 909, Chicago 1, Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE, Congress Hotel, Chicago, Nov. 15-17. Dr. Quentin M. Geiman, 25 Shattuck St., Boston 15, Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 14-15. Dr. Clarence C. Hare, 170 Maple Ave., White Plains, N. Y., Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, French Lick Springs Hotel, French Lick, Ind., Oct. 29-31. Dr. Dean F. Smiley, 185 N. Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICERS, Washington, D. C., Nov. 26-30. Dr. John D. Porterfield, 306 Ohio Depts. Bldg., Columbus 15, Ohio, Secretary.

CENTRAL NEUROPSYCHIATRIC ASSOCIATION, Hotel Nicollet, Minneapolis, Oct. 19-20. Dr. Lee M. Eaton, 102 Second Ave. S.W., Rochester, Minn., Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH, Drake Hotel, Chicago, Nov. 2-3. Dr. Kenneth G. Kohlstaedt, 960 Locke St., Indianapolis 7, Secretary.

INDIANA STATE MEDICAL ASSOCIATION, Indianapolis, Oct. 29-31. Miss Lucille Kribs, 23 E. Ohio St., Indianapolis 4, Acting Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, St. Louis, Oct. 22-26. Dr. Tom B. Throckmorton, Equitable Bldg., Des Moines, Iowa, Secretary.

NATIONAL ASSOCIATION OF CLINIC MANAGERS, Buena Vista Hotel, Biloxi, Miss., Oct. 29-31. Mr. Floyd R. Detert, Marshfield Clinic, Marshfield, Wis., Secretary.

NORTH PACIFIC SURGICAL ASSOCIATION, Vancouver, B. C., Canada, Nov. 16-17. Dr J. A. Duncan, 509 Olive Way, Seattle, Wash., Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Biltmore Hotel, Oklahoma City, Oct. 29-Nov. 1. Mrs. Muriel R. Waller, 612 Medical Arts Bldg., Oklahoma City, Executive Secretary.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 29-Nov. 2. Dr. L. E Moon, 1031 Medical Arts Bldg., Omaha 2, Secretary.

PUERTO RICO MEDICAL ASSOCIATION, Santurce, Dec. 12-16. Dr. Victor J. Montilla, P. O. Box 3866, Santurce, Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Chicago, Dec. 3-7. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary.

SOUTHERN MEDICAL ASSOCIATION, Dallas, Texas, Nov. 5-8. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHERN SURGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Dec. 4-6. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

WESTERN SURGICAL ASSOCIATION, Broadmoor Hotel, Colorado Springs, Colo., Nov. 29-Dec. 1. Dr. Michael L. Mason, 154 E. Erie St., Chicago 11, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, Mexico City, Mexico, Dec. 11-19. Mrs. Grace E. O'Neill, Division of World Affairs, National Association on Mental Health, 1790 Broadway, New York 19, N. Y.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2. England, Hon. Secretary.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Mexico City, Mexico, Jan. 6-12. Dr. Luis Sanchez Bulnes, Gomez Farias 19, Mexico 4, D.F., Secretary-General.

PAN AMERICAN CONGRESS OF PEDIATRICS, Montevideo, Uruguay, Dec 5-8. Dr. Maria Luisa Saldien de Rodriguez, Avenida 18 de Julio, 1246, Montevideo, Uruguay, General Secretary.

PAN PACIFIC SURGICAL ASSOCIATION CONGRESS, Honolulu, Hawaii, Nov. 7-19. Dr. Forrest J. Pinkerton, Suite 7, Young Bldg., Honolulu, Hawaii, President.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* All centers where there are five or more candidates. Final date for filing application is Dec. 17. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Various Locations, July 18. Final date for filing application is Jan. 18. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Chicago, March 1952. *Oral.* Chicago, May 1952. Final date for filing application is Feb. 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various centers, Oct. 15. Final date for filing applications was May 1. *Oral.* The schedule of oral examinations for 1951 has been arranged on a regional basis as follows: New York, Nov. 12-14, covering Maine, Massachusetts, New Hampshire, New York and Vermont. San Francisco, Oct. 22-24, covering Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. Final date for filing applications was Sept. 1.

Oral examinations in the subspecialties will be held at the same time and place and on the same distribution.

Subspecialty examination in Gastroenterology. San Francisco, Oct. 19 and Buffalo, N. Y., Nov. 19.

Exec. Sec., Dr. William A. Werrell, 1 W. Main St., Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New Haven, Oct. 25-26 *Oral* Chicago, May 1952. Final date for filing applications for the May 1952 examination is Jan. 1, 1952. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written.* Feb. 1, 1952. Final date for filing applications is Nov. 1. *Oral.* Chicago, June 9-13, 1952. Final date for filing applicaiuon is Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Twenty-five centers, Feb. 4-5, 1952. Sec., Dr. Edwin B. Dumphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Final date for filing applications for the 1952 Part II examinations was Aug. 15. Final date for filing application for the 1952 Part I examination is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF PEDIATRICS: Written examination under local monitors, Jan. 11. This is the only written examination which will be given during 1952. *Oral.* New York City, Feb. 1-3; St. Louis, Mo., April; Washington, D. C., May 3-5; San Francisco, late June; Chicago, October and Boston, late November. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II.* Chicago, June. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: Denver, Oct. 27-29. Final date for filing of case reports was Aug. 30. Sec., Dr. Bradford Cannon. Office of the Board: 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Written.* San Francisco, October 28. *Oral.* San Francisco, October 29. Sec., Dr. Ernest L. Stebbins, 615 North Wolfe St., Baltimore 5.

AMERICAN BOARD OF PROCTOLOGY: Philadelphia, Nov. 17-18. Sec., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERCIAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral* New York, Dec. 17-18. Final date for filing applications was Sept. 1. Act. Sec., Dr. David A. Boyd Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers. March 1952. Final date for filing application is Dec. 1, 1951. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

BOARD OF THORACIC SURGERY: *Oral.* St. Louis, Nov. 2. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 9-13, 1952. Final date for filing applications was Sept. 1. Sec., Dr. Harry Culver, 30 Westwood Rd., Minneapolis 16.

DEATHS

McNamee, Edgar Paul ✙ Cleveland; born in Butler, Pa., June 29, 1890; University of Pennsylvania School of Medicine, Philadelphia, 1913; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, of which he had been president, and the American College of Radiology, of which he had been vice-president; fellow of the American College of Physicians; past president and secretary of the Cleveland Radiological Society; president of the Ohio State Medical Association in 1946 and 1947; member of the House of Delegates of the American Medical Association from 1946 to 1951; served during World War I; for six years a member of the board of directors of the Academy of Medicine of Cleveland; member of a committee of five selected by Governor Lausche to attend a course at Western Reserve University in the treatment of atom bomb injuries; head of the radiology department, which he established in 1920 in St. Alexis Hospital, where he died July 8, aged 61, of bronchopneumonia.

Cole, Paul Fremont ✙ Springfield, Mo.; born Aug. 24, 1880, in Steffenville, Mo.; Barnes Medical College, St. Louis, 1905; also a pharmacist; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; served overseas during World War I; past president of the Greene County Medical Society; conducted a column known as "Ozark Doc" in the medical society's *Bulletin,* which he founded as a private enterprise before turning it over to the Greene County Medical Society and becoming editor emeritus; with the profits he made, started the Greene County Medical Society Building Fund; on the staffs of St. John's Hospital and the Medical Center of Federal Prisoners; died July 13, aged 70.

Fletcher, Harold Augustus ✙ Kentfield, Calif.; born in Alpena, Mich., Dec. 10, 1888; Stanford University School of Medicine, San Francisco, 1916; formerly associate clinical professor of surgery (otorhinolaryngology) at his alma mater; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society, American Otological Society, and the Pacific Coast Oto-Ophthalmological Society; past president of the San Francisco County Medical Society and of the San Francisco Chapter of the League for the Hard of Hearing; served in France during World War I; chairman of the California Procurement and Assignment Service during World War II; affiliated with Stanford University Hospitals; died July 26, aged 62, of coronary thrombosis.

McGovern, Francis Xavier ✙ Washington, D. C.; born in New York Dec. 26, 1893; Fordham University School of Medicine, New York, 1916; served during World War I; formerly affiliated with the U. S. Public Health Service Reserve; member of the medical advisory council of the National Selective Service System in 1940 and in 1941 chairman of the local procurement and assignment service for physicians in the war manpower commission; affiliated with the Garfield Memorial Hospital; for many years chairman of the executive committee of the Medical Society of the District of Columbia, which in 1942 presented him with the society's Certificate of Award for Meritorious Service; died in Veterans Administration Hospital, Mt. Alto, July 28, aged 57, of homologous serum hepatitis.

Ward, Edwin St. John ✙ Penney Farms, Fla.; born in Brookline, Mass., March 31, 1880; Columbia University College of Physicians and Surgeons, New York, 1904; member of the Massachusetts Medical Society; fellow of the American College of Surgeons; formerly a medical missionary; served with the Congregational Christian American Board of Commissioners for Foreign Missions in Turkey from 1907 to 1911; at one time dean and professor of surgery at the American University of Beirut School of Medicine in Beirut, Syria; served as medical director at the Hospital Cottages for Children in Baldwinsville, Mass.; pathologist at Henry Heywood Memorial Hospital in Gardner, Mass., Mary Lane Hospital in Ware, Mass., and Leominster (Mass.) Hospital; died in Northampton, Mass., July 31, aged 71, of cerebral hemorrhage and arteriosclerosis.

Wilcox, Henry Williams, Santa Barbara, Calif.; born in Hartford, Conn., July 9, 1868; Colorado School of Medicine, Boulder, 1897; associate professor of orthopedic surgery, emeritus, at his alma mater, now known as the University of Colorado School of Medicine in Denver, where he practiced for many years and was affiliated with Denver General, St. Luke's, St. Anthony's, National Jewish, Beth Israel, and Presbyterian hospitals; specialist certified by the American Board of Orthopaedic Surgery; member of the American Medical Association and the Colorado State Medical Society; fellow of the American Academy of Orthopaedic Surgeons and the American College of Surgeons; died July 25, aged 83, of coronary occlusion.

Togus, L. Theodore, Manchester, N. H.; born in Hooksett, N. H., Nov. 6, 1880; University of Vermont College of Medicine, Burlington, 1909; member of the American Medical Association, American Academy of Ophthalmology and Otolaryngology and the New England Otolaryngological Society; specialist certified by the American Board of Otolaryngology; served during World War I and later as a major in the medical reserve corps; at one time a member of the school board and board of trustees of the public library in Hooksett; for many years on the staff of Elliot Hospital; affiliated with the Veterans Administration Hospital, where he died July 14, aged 70, of cerebral hemorrhage.

Alder, George Byron, Chattanooga, Tenn.; University of Nashville Medical Department, 1909; member of the American Medical Association; on the staff of Erlanger Hospital, where he died Aug. 7, aged 65, of coronary disease.

Ashley, Robert Grady, Mayfield, Ky.; Vanderbilt University School of Medicine, Nashville, Tenn., 1921; member of the American Medical Association; died in Madisonville Aug. 5, aged 56, of tuberculosis.

Beck, Frederick Oswald, Omaha; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the American Medical Association; died Aug. 1, aged 71, of coronary occlusion.

Behrman, Oscar, Cincinnati; Medical College of Ohio, Cincinnati, 1904; member of the American Medical Association; died in Jewish Hospital Aug. 10, aged 68, of hepatic metastases and rectal carcinoma.

Beltzer, Charles Eugene ✙ Washoe, Mont.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; served during the Spanish American War and World War I; died Aug. 7, aged 71, of carcinoma.

Caldwell, Herbert, St. Petersburg, Fla.; Hospital College of Medicine, Louisville, Ky., 1906; served on the staffs of various Veterans Administration hospitals; died Aug. 15, aged 75, of coronary thrombosis.

Cattley, Stephen James ✙ Ogdensburg, N. Y.; New York Homeopathic Medical College and Hospital, New York, 1917; past president of St. Lawrence County Medical Society; served as a captain with the British Army in a base hospital at Archangel, Russia, during the Allied occupation of Northern Russia; a member of the visiting staff of the St. Lawrence State Hospital; past president of the medical staff of the A. Barton Hepburn Hospital; died recently, aged 66, of coronary occlusion.

Chiles, Joseph Haskell ✙ Orlando, Fla.; University College of Medicine, Richmond, 1905; served during World War I; formerly city and county physician; died Aug. 6, aged 74, of myocardial infarction.

✙ Indicates Fellow of the American Medical Association.

V 14
1951

Dagg, Thomas Levi, Chicago; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; formerly on the staff of St. Luke's Hospital; served during World War I; died in Wesley Memorial Hospital Aug. 9, aged 83, of arteriosclerotic heart disease.

Dawson, Charles Arthur ✠ River Falls, Wis.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1903; since 1943 secretary of the state board of medical examiners, of which he became a member in 1941; past president of the State Medical Society of Wisconsin; served during World War I; a member and in 1947 chairman of the state board of veterans affairs; chief of staff, City Hospital; died in New Richmond Aug. 9, aged 70, of heart disease.

Dawson, John William ✠ El Dorado Springs, Mo.; St. Louis College of Physicians and Surgeons, 1896; an Associate Fellow of the American Medical Association; died July 20, aged 78, of myocarditis.

Denno, Willard Joseph ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1906; fellow of the American College of Physicians; served as attending physician of the tuberculosis clinics and as assistant to the director of the division of tuberculosis, city health department; medical director of the Standard Oil Company until he retired Dec. 31, 1945; died Aug. 29, aged 75, of cerebral hemorrhage.

De Vall, Frederick Clayton ✠ Garretson, S. D.; Sioux City College of Medicine, 1905; died in Sioux Valley Hospital, Sioux Falls, Aug. 16, aged 72.

Dougherty, Gerald Luke, Wilmington, Del.; University of Maryland School of Medicine, Baltimore, 1908; member of the American Medical Association; served during World War I; on the staff of St. Francis Hospital, where he died Aug. 9, aged 70, of myocardial infarction.

Duckworth, Guilford Marvin, Cuero, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; member of the American Medical Association; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; past president of the DeWitt County Medical Society; died in Charlotte, N. C., Aug. 3, aged 73, of hemorrhage and cirrhosis of the liver.

Dudley, Charles, Kingston, Mass.; Harvard Medical School, Boston, 1897; member of the American Medical Association; died June 28, aged 82, of arteriosclerosis and gastric ulcer.

Dyer, Harry Cheney, Pomona, Calif.; Gross Medical College, Denver, 1900; died Aug. 19, aged 76.

Eaddy, Julius Davis, Florence, S. C.; Medical College of the State of South Carolina, Charleston, 1905; served in France during World War I; died Aug. 1, aged 68, of coronary occlusion.

Endres, Joseph Mathias, Havertown, Pa.; Medico-Chirurgical College of Philadelphia, 1912; member of the American Medical Association; formerly on the staff of St. Agnes Hospital; died Aug. 15, aged 65.

Fabricius, Julius Robert ✠ Pittsburgh; Bellevue Hospital Medical College, New York, 1892; an Associate Fellow of the American Medical Association; member of the Medical Society of the State of New York; died July 23, aged 79, of coronary thrombosis.

Farrow, Joseph, Spokane, Wash.; M. B., University of Toronto Faculty of Medicine, 1892; Victoria University Medical Department, Coburg, Ont., Canada, 1892; member of the American Medical Association; on the staffs of St. Luke's and Sacred Heart hospitals; died Aug. 16, aged 86, of heart disease.

Field, Clarence Everett, Manhasset, N. Y.; University of the City of New York Medical Department, New York, 1891; died in Highlands, N. J., Aug. 3, aged 81, of pneumonia.

Foshion, Herbert Victor, Algoma, Wis.; University of Minnesota Medical School, Minneapolis, 1924; member of the school board; affiliated with Door County Memorial Hospital in Sturgeon Bay, St. Mary's and Bellin Memorial hospitals in Green Bay, and the Algoma Hospital; died in Wisconsin General Hospital, Madison, July 25, aged 56, of cerebral hemorrhage, following an operation for trigeminal neuralgia.

Franke, William E., Newton, Ill.; St. Louis College of Physicians and Surgeons, 1892; member of the American Medical Association; died in St. John's Hospital, Springfield, Aug. 4, aged 81, of carcinoma of the gallbladder.

Gay, Joseph Reid ✠ Waycross, Ga.; University of Georgia School of Medicine, Augusta, 1935; served during World War II; died in the Veterans Administration Hospital, Dublin, in August, aged 54.

Gibney, Ernest Carson, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1895; formerly on the staff of the Hospital for Ruptured and Crippled; died in General Hospital of Monroe County, East Stroudsburg, Pa., Aug. 6, aged 83, of cardiovascular disease and mesenteric thrombosis.

Hardy, Periam Burrows ✠ Tecumseh, Mich.; Long Island College Hospital, Brooklyn, 1892; past president of the Lenawee County Medical Society; affiliated with the Emma L. Bixby Hospital in Adrian, and Herrick Memorial Hospital, where he died Aug. 5, aged 81, of cerebral hemorrhage.

Haviland, Clarence Merritt, San Diego, Calif.; University of Southern California School of Medicine, Los Angeles, 1894; died Aug. 12, aged 87.

Hutchison, Lorenzo D., England, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1920; died in St. Vincent's Hospital, Little Rock, Aug. 5, aged 62, of heart disease.

Jackson, Earl Holcomb, Schenectady, N. Y.; Albany Medical College, 1902; formerly county coroner; served during World War I; died in St. Clare's Hospital July 29, aged 72, of coronary thrombosis.

Jones, Marion Jacobs, Portland, Ore.; University of Oregon Medical School, Portland, 1910; member of the American Medical Association; served in France during World War I; for many years affiliated with Emanuel Hospital; died July 30, aged 69, of coronary disease.

Kirkwood, Allan Stewart, Montclair, N. J.; University and Bellevue Hospital Medical College, New York, 1913; member of the American Medical Association; past president of the Associated Physicians of Montclair and Vicinity; affiliated with Mountainside Hospital, where he died July 28, aged 80, of coronary thrombosis.

Krieger, William Arnold, Newport, Ky.; University of Louisville Medical Department, 1909; member of the American Medical Association; served in France during World War I; on the examining board of Selective Service during World War II; for many years on the staff of Speers Memorial Hospital in Dayton; formerly health officer and city physician; died in the Veterans Administration Hospital, Fort Thomas, July 28, aged 63, of lobar pneumonia.

Lackey, William Nicholas, Gallatin, Tenn.; Jefferson Medical College of Philadelphia, 1899; city health officer; served during World War I; died in the Veterans Administration Hospital, Murfreesboro, July 18, aged 75, of encephalomalacia due to arteriosclerosis.

Lashman, William Mitchell, Camden, N. J.; Jefferson Medical College of Philadelphia, 1912; first president of South Jersey Medical Society; died in Jefferson Hospital, Philadelphia, July 21, aged 62, of fibrosarcoma.

Latham, James Ryder, Orlando, Fla.; University of the City of New York Medical Department, 1879; died July 29, aged 96, of cerebral arteriosclerosis.

Leach, George A., Morris, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1901; also a pharmacist; on the staff of Morris Hospital; died July 21, aged 88, of cerebral hemorrhage.

Lee, Gisle Martin, Thompson, Iowa; Rush Medical College, Chicago, 1893; member of the American Medical Association; died in Forest City (Iowa) Municipal Hospital July 14, aged 84, of cerebral vascular accident.

Leo, Robert Albert, Newport, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1919; died July 27, aged 59.

Lynch, Daniel Bernard ✠ Albany, N. Y.; University and Bellevue Hospital Medical College, New York, 1916; served in France during World War I; a member of draft board 343 during World War II; awarded an honorary doctor of letters degree from Siena College, Loudonville, in June 1951; on the staff of Albany Hospital and for many years on the staff of St. Peter's Hospital, where he died July 21, aged 59, of amyotrophic lateral sclerosis.

McCarter, Harry Chandley, Beaver Falls, Pa.; University of Pittsburgh School of Medicine, 1920; member of the American Medical Association; served during World War I; for many years county coroner and school physician; county medical director and appointee of Civil Service Board; on the staffs of Beaver Valley General Hospital in New Brighton and the Providence Hospital, where he died Aug. 16, aged 58.

McCaskey, George Hadden, Winamac, Ind.; Indiana University School of Medicine, Indianapolis, 1911; member of the American Medical Association; affiliated with St. Joseph Hospital in Logansport, where he died July 25, aged 64, of coronary thrombosis.

Mace, Lewis Sayre ✠ Los Gatos, Calif.; University and Bellevue Hospital Medical College, New York, 1899; an associate Fellow of the American Medical Association; for many years practiced in San Francisco, where he was on the faculty of the University of California Medical School, and served on the health commission; died July 14, aged 80, of carcinoma of the prostate.

MacKenzie, Alexander Ross, Huntington, W. Va.; University of Maryland School of Medicine, Baltimore, 1910; member of the Radiological Society of North America and the American Medical Association; radiological consultant for St. Mary's and Chesapeake and Ohio hospitals; died July 18, aged 65, of coronary thrombosis.

May, R. Cameron ✠ Cornwall-on-the-Hudson, N. Y.; Syracuse University College of Medicine, 1932; served during World War II; on the staff of Cornwall Hospital; died recently, aged 46, of cerebral embolism.

Merrill, William Truman, Milton, Mass.; Medical School of Maine, Portland, 1890; Dartmouth Medical School, Hanover, N. H., 1890; member of the American Medical Association and the Connecticut State Medical Society; joined the U. S. War Risk Bureau and later the Veterans Administration; died in Milton (Mass.) Hospital July 11, aged 90, of arteriosclerotic heart disease.

Phipps, Joseph Allen, Salt Lake City; Marion-Sims College of Medicine, St. Louis, 1898; member of the American Medical Association; fellow of the American College of Surgeons; served on the staffs of Holy Cross Hospital, Salt Lake County General Hospital, and the Dr. W. H. Groves Latter-Day Saints Hospital; died Aug. 1, aged 85, of myocardial infarction due to arteriosclerosis.

Powell, Harley Jesse, Bowling Green, Ohio; Western Reserve University Medical Department, Cleveland, 1908; for many years county health commissioner; served during World War I; died in Community Hospital July 22, aged 80, of cerebral hemorrhage.

Powell, Jay A., West Palm Beach, Fla.; University of Oklahoma School of Medicine, Oklahoma City, 1918; member of the American Medical Association and the Southeastern Surgical Congress; died July 2, aged 58, of coronary thrombosis.

Purvin, Myles, Long Beach, Calif.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1895; also a graduate in law; served as director of communicable diseases for the New York City Health Department; died July 25, aged 77, of cardiac failure and diabetes mellitus.

Richeson, Vern N., Flint, Mich.; Detroit College of Medicine, 1916; member of the American Medical Association; served in France during World War I; died in Hurley Hospital July 25, aged 61, of coronary thrombosis.

Rosasco, John Loring, San Francisco; Stanford University School of Medicine, San Francisco, 1933; served during World War II; died July 30, aged 44, of coronary arteriosclerosis.

Schlieker, Alexander Grant ✠ Troy, Mo.; Independent Medical College, Chicago, 1899; Northwestern University Medical School, Chicago, 1900; an Associate Fellow of the American Medical Association; member of the Indiana State Medical Association; fellow of the American College of Surgeons; formerly practiced in East Chicago, Ind., where he was on the staff of St. Catherine's Hospital; died in the Veterans Administration Hospital, Hines, Ill., July 14, aged 83.

Scott, Frederick Hughes, Minneapolis; University of Toronto Faculty of Medicine, Toronto, Canada, 1904; an Associate Fellow of the American Medical Association; professor emeritus of physiology at the University of Minnesota Medical School; died July 21, aged 75, of cerebral hemorrhage.

Sheppard, Thomas Stathem, Millville, N. J.; Maryland Medical College, Baltimore, 1913; member of the American Medical Association; died July 28, aged 61, of coronary occlusion.

Smiseth, Selmer Pareli ✠ St. Petersburg, Fla.; University of Michigan Medical School, Ann Arbor, 1924; died in Munson Hospital, Traverse City, July 21, aged 56, of ruptured abdominal aneurysm.

Smith, Frank W., ✠ Chestertown, Md.; Baltimore Medical College, 1900; served as vice-president of the Medical and Chirurgical Faculty of Maryland and Kent County Medical Society; served as county register of wills; vice-president of the Kent County Savings Bank; chief of staff, Kent and Upper Queen Anne's General Hospital, where he died July 16, aged 71, of coronary occlusion.

Smith, Irvine M., Milwaukie, Ore.; Willamette University Medical Department, Salem, 1892; served as health officer of Tillamook County; died in Portland Sanitarium and Hospital in Portland, July 4, aged 88, of cardiovascular renal disease.

Smith, Wesley Sydney ✠ San Diego, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1933; served in the Pacific theater during World War II; formerly president of the alumni association of his alma mater; died in Glendale Sanitarium and Hospital in Glendale, July 22, aged 43, of lymphosarcoma.

Spangler, Clayton Valentine, Northampton, Pa.; Eclectic Medical College, Cincinnati, 1923; member of the American Medical Association; served as a member of the school board, of which he had been treasurer; died July 28, aged 55, of injuries received in an automobile accident.

Steinman, Henry Edward ✠ Monroeville, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; on the visiting staff of St. Joseph's, Methodist, and Lutheran hospitals in Fort Wayne, and the Adams County Memorial Hospital in Decatur; served during World War I; president of the First Citizens State Bank; died July 17, aged 70, of coronary occlusion.

Teitz, Leo, Cincinnati; Julius-Maximilians-Universität Medizinische Fakultät, Wurzburg, Bavaria, Germany, 1915; member of the American Medical Association; a physician for the board of education; on the staff of Jewish Hospital, where he died July 11, aged 59, of shock following a cystoscopy.

Wallace, James Marvin, Johnson City, Tenn.; Vanderbilt University School of Medicine, Nashville, 1899; served on the staffs of various Veterans Administration hospitals; died in Tampa, Fla., July 14, aged 73, of coronary sclerosis.

Whisler, Lehr Harrison, Willard, Ohio; Ohio State University College of Medicine, Columbus, 1914; served during World War I; formerly member of the city council; affiliated with Willard Municipal Hospital, where he died July 15, aged 62, of cerebral hemorrhage.

White, Arthur D., Two Rivers, Wis.; University of Buffalo School of Medicine, 1893; for many years practiced in Ithaca, N. Y., where he was affiliated with Ithaca Hospital, died July 26, aged 80, of heart failure.

Wier, Austin K., Ranger, Texas (licensed in Texas under the Act of 1907); member of the American Medical Association; past president of the Eastland-Callahan Counties Medical Society; served as county health officer; health officer of Ranger; affiliated with Ranger General Hospital; died recently, aged 73, of coronary occlusion.

V 14
1951

GOVERNMENT SERVICES

NAVY

Health of the Navy.—During the year 1950 the Navy Medical Department was faced with the task of readjustment incident to rebuilding and mobilization. Medical facilities, personnel, and equipment had to be augmented to care for a rapidly increasing military service. Mobilization meant that hundreds of thousands of physical examinations and millions of immunizations would be given, many health and training programs would be formulated, and medical research would be extended to encompass epidemiological factors associated with warfare in a foreign terrain. During the first seven months of 1950, just prior to the military expansion, the decreasing trend in rates for morbidity continued to the extent that new records would undoubtedly have been established if the Korean situation had not occurred.

Final data for 1950 show an over-all incidence rate (including battle casualties) of 348.0 per 1,000 average strength, as compared to 347.2 for the preceding year. In other words, the incidence rate for 1950 almost equalled the record rate for the preceding year even though all battle injuries and other related morbidity are included. The over-all incidence rate is calculated from data on communicable and other diseases and accidents, violence, and poisonings. In considering these groups, with battle casualties excluded, only the incidence rate for accidents, violence, and poisonings increased over the rate for 1949, 53.7 per 1,000 as compared to 47.1. Much of the improvement was owing to the reduction in communicable diseases and related conditions, which declined 10%. The rate for the remaining diseases decreased from 164.5 per 1,000 in 1949 to 158.2. The incidence of venereal diseases also continued to decline from a rate of 43.1 per 1,000 in 1949 to 40.7 in 1950; the sick days per case and noneffective rate likewise declined.

The experience in 1950 was comparable to that of 1949 in most respects when casualty data are omitted. For example, the noneffective rate per 1,000 was 18.7 in 1950 and 18.6 in 1949. The average number of sick days per person in the naval service was 6.8 in both years, and the average number of sick days per case was 20.4 in 1950 as compared to 19.6 in the previous year.

The death rate, which had been decreasing steadily since 1943, increased to 2.15 per 1,000, about the same level as 1945. Out of 1,155 noncombat fatalities during 1950, 922 (80%) were owing to accidents, violence, and poisonings, about the same proportion as in 1949.

The rate of invalidings from the service increased from the previous year, 10.2 per 1,000 as compared to 6.7. During 1950 a total of 5,516 individuals were separated from the service for medical reasons, with about one-half of these being separated under the terms of the Career Compensation Act of 1949.

The average daily hospital census of patients of all types was 14,316 in 1950 as compared to an average of 13,920 hospital patients the preceding year. The average daily hospital census of supernumerary patients declined 7%, while the average number of active-duty patients hospitalized each day increased about 10%. A comparison of these averages, however, does not reveal the rapid increase in the hospital load that occurred in the last few months of the year. At the beginning of the last quarter the total hospital census was 14,595, and three months later it had increased to 20,373. All of this increase was contributed by active-duty Navy and Marine Corps personnel.

The utilization of naval hospitals by patients of the Army and Air Force reached its peak in October, 1950, when over 4,000 were using naval medical facilities. About 2,500 of these patients were combat casualties. The number of Navy and Marine Corps patients in hospitals of the other military services reached a peak of 1,400 in December, 1950. Most of the Army and Air Force patients were in continental naval hospitals, while the majority of Navy and Marine Corps patients using the facilities of the other services were overseas.

To get an accurate picture of morbidity in 1950 one must include the battle casualties. For every combat casualty treated there were 24 noncombat cases. Out of every 20 sick days accumulated by patients, 1 day was for a battle injury. In addition, 6 of every 10 deaths during 1950 were owing to enemy action. It was only in the death rates that combat casualties materially altered the favorable morbidity comparisons between the years 1949 and 1950.

During the first half of 1951, the incidence of illness in the Navy increased. The rate of admissions to the sick list rose to 563 per 1,000 strength in February, the highest rate for any one month since March, 1947, and 71% above the same month of 1950. While the admission rates declined beginning with March, these rates were about one-fifth higher than the comparable months of the previous year. While there is little doubt that battle casualties have some influence on the current increase in rates, a more important factor is associated with the increase in Naval population, incident to mobilization, and consequently in the prevalence of respiratory ailments. Upper respiratory ailments in the continental United States alone accounted for almost three-fourths of the increase over 1950. The rate for injuries during the period January-June of 1950 and 1951 were about the same. During 1951, a peak in the average hospital census was revealed in February with 22,466 patients. The next four months saw a slight decrease in this census. This was due mainly to the steady decrease in supernumeraries hospitalized, which started in October, 1950. On the other hand, the census of active-duty patients in June was about the same as for February, the peak month. The number of sick days amassed by active-duty patients on the sick list during the first six months of 1951 has almost reached the total accumulated during the entire 1950. The estimated rate of noneffectiveness was 26 per 1,000 strength during this half year, about one-fourth above that of 1950.

Instruction in Radioactive Isotopes.—A six-day course of instruction in medical aspects of special weapons and radioactive isotopes will begin Nov. 26, 1951, at the Naval Medical School, Bethesda, Md. The course, the first in fiscal year 1952, is given primarily for inactive medical department officers of the Naval Reserve. Problems most likely to be encountered by medical personnel and techniques to be employed by them in the field of radioactivity will be discussed during the instruction period. The various subjects will be presented by guest speakers, each prominent in his specialty.

Medical, dental, medical service corps, and nurse corps officers of the Inactive Reserve residing in the first, third, fourth, fifth, sixth, eighth, and ninth Naval Districts and the Potomac River Naval Command who wish this instruction should submit their request for the six-day period of training duty to the commandant of their respective Naval District at once. Acceptance of orders to attend the course of instruction will in no way increase the possibility of involuntary recall to active duty. Messing facilities are available. A limited number of sleeping quarters are available and will be filled on the first come first served basis.

Tuberculosis Decreases in Navy Civilian Employees.—The results of the Navy's civilian employee Chest X-ray Program for the calendar year ending Dec. 31, 1950, indicate that the incidence rate of suspected tuberculosis among the civilian employees of the Navy Department continued to decrease for the third consecutive year.

Of the 222,122 chest x-ray films viewed, 603 were suspected of indicating tuberculosis and 609 indicated other questionable nontuberculous conditions. Under the Navy's Tuberculosis Control Program, 1,212 persons were referred to their family physicians for further clinical study. Thus, earlier diagnosis and effective treatment can be provided to the employee than would have been possible after noticeable symptoms developed.

Chest x-rays, by means of photofluorographic equipment, are made annually on all Navy civil employees, and at the time of their entering and leaving naval employment.

FOREIGN LETTERS

PARIS

International Congress of Military Medicine.—The International Congress of Military Medicine and Military Pharmacy convened for the thirteenth time—for the second time in Paris—under the sponsorship of the President of the French Republic and under the chairmanship of General Jame, inspector-physician. General Dutrey, M.C., was secretary. This successful meeting was attended by delegates from 43 nations. There were 1,800 participants in the congress. These congresses grew out of the Inter-Allied Conferences of War Surgery, which the French Health Service organized in Val-de-Grâce during World War I.

The inaugural session of the congress was held in the Great Amphitheater of the Sorbonne. The retiring president, Gen. Landero Ramírez of Mexico, stressed the international altruism that constitutes the first professional duty of the military physician. After him, General Jame, who is also director general of the Health Services of the Armies and president of the International Committee on Military Medicine and Military Pharmacy, welcomed the congress and reviewed the history of military medicine. He recalled the great names that brought fame to the "École d'Application" of Val-de-Grâce, which has left its imprint on all the activities of military physicians. He then reviewed the results of the work of the International Committee of Military Medicine and Military Pharmacy, which has succeeded in laying the foundations of an international medical law.

Problems studied at the business sessions were: (1) tactical and material organization of emergency aid in case of a mass influx of wounded following an attack on large communities; (2) organization of instruction of medical corps personnel (active as well as reserve) and planning of the medicomilitary career; (3) medical problems arising from air and submarine navigation; (4) medical aspects of the defense against atomic, bacteriologic, and chemical warfare; and (5) present interpretation of the role of military pharmacy in time of war.

Gen. Guillermo Rodríguez Guerrero conveyed at the closing session the invitation of the Uruguayan government to hold the 14th congress in Montevideo in 1953. The following subjects were put on the agenda of that congress: (1) military medicine considered as a specialty (reports by the United States and Uruguay); (2) national medical organization in wartime; coordination of civil and military services; preparation in peacetime (reports by Yugoslavia and Uruguay); (3) functioning of the health service in war in high mountains (reports by Switzerland and Norway); and (4) modern concept of treatment of burned and wounded persons in the front lines (reports by Benelux and Uruguay).

The subject of the pharmacy section will be organization and tasks of pharmaceutical military corps and the instruction of reserve personnel (reports by Brazil and Uruguay), and the subject of the dental section will be the establishment of a standard dental code for treatment of military personnel and possibly for identification of soldiers (reports by Canada and Uruguay).

There was an interesting and successful exhibit of arts and sciences applied to medicine, surgery, pharmacy, and sanitary hygiene, as well as an exhibit of the new achievements of the services of the French military health services (land, sea, and air) in the gardens of Val-de-Grâce. As a tribute to military medicine, a special stamp, sold within the gates of Val-de-Grâce, was issued.

M. Vincent Auriol, President of the French Republic, honored the chiefs of the delegations by receiving them at "L'Élysée."

The items in these letters are contributed by regular correspondents in the various foreign countries.

Following the Congress of Military Medicine and Military Pharmacy, the fourteenth session of the International Office for Documentation of Military Medicine was held, on June 24 and 25, in Vichy. Two important subjects, which had been studied by international surveys, were reported on. The first, discussed by General des Cilleuls, concerned the identification of medical personnel, and the second, presented by Chief Surgeon First Class Puyo, concerned the release of health service and religious personnel held with prisoners of war.

A group of 15 delegates made a motion for the study of a new problem; limitations of medicine in biologic warfare, by the International Committee of Military Medicine and Military Pharmacy.

Treatment of Cirrhosis with Perfusions of Ascitic Fluid.—The ascitic form of hepatic cirrhosis is commonest in France, owing to the fact that a large number of cases are connected with slow and prolonged intoxication by absorption of wine. In 1949, Prof. E. Chabrol, A. Giraud, and P. Fallot proposed a treatment by autoperfusion of ascitic fluid to replace the loss of albumin. Intravenous injections were well tolerated, provided that the perfusate did not contain pyrogenic substances. Ascitic fluid is gathered aseptically in 500 cc. sterile bottles containing 5 cc. of 10% sodium citrate. The bottles, refrigerated and under bacteriological control, can be kept for eight days. Two different techniques have been tried: (1) daily injections of 500 cc. and (2) injection of large doses ranging from 1.5 to 2 liters, by intravenous drip at average intervals of four to five days. The first method was used in 15 patients, in 5 of whom the treatment brought about a regression of ascites and edema. The second method gave better results. Among the 12 cases thus treated, the authors noted 2 cases of lasting resorption of edema and 8 cases of considerable improvement. Advantages of ascitic autoperfusion over the classic methods, with use of glucose and human serums, include the production of an important urinary output without introduction of supplementary fluid. According to the authors, this treatment significantly improved the prognosis in cirrhosis: in 1,000 patients treated by the authors in 30 years with the classic methods, 4 to 5% of recoveries were noted, whereas the autoperfusion treatment produced 10% recoveries. The authors consider three hypotheses to explain the resorption of edema and ascites with this new treatment: (1) the restoration of osmotic pressure, (2) the increase of blood volume, and (3) the administration of a possible hormone or an anti-hormone favoring diuresis.

J. Caroli and A. Paraf dealt with the problem of ascites that persists despite repeated tapping. During periods of attack they recommend daily punctures for 12 to 15 days with the removal of 2,500 to 3,000 cc. during each puncture. During the maintenance period they continue drawing every day or every other day a quantity of fluid equal to that occurring in the interval between punctures, which varies between 1,000 and 1,500 cc. if the patient is on an unrestricted diet and is less if he is on a salt-free diet. This treatment necessitates hospitalization and absolute asepsis; the operation is performed with a small trocar (Küss type). Results are excellent, and the general condition is greatly improved. The patient may be fed adequately with Patek's diet, which is rich in proteins and has a high caloric content, compensating for the often enormous protein losses (up to 1,100 gm.) within 6 to 8 months. With this treatment, most patients are able to resume their customary activity.

Evolution of Alcoholism.—Professor Derobert presented a review of the evolution of alcoholism in the *Bulletin national d'hygiène*. There is no doubt that there is a recrudescence of alcoholism in France. In consideration of the danger that this represents for public health, the national Academy of Medicine recently protested to the government against the decision to allow the sale of certain drinks with a high alcoholic content.

V 14
1951

Cortisone and Infantile Eczema.—At the clinic of the Hospital for Sick Children, Prof. Robert Debré and his associates, P. Mozziconacci and M. K. Caramanian, have treated infantile eczema with cortisone. Results were encouraging: cutaneous lesions subsided after a few days' treatment, and a maintenance course of one or two injections per week prevented the otherwise constantly recurring relapses. Toxic effects of treatment were pulmonary edema and arterial hypertension. In cases in which there was much infection, antibiotics were used with cortisone; cortisone in itself did not aggravate infection. Corticotropin (ACTH) produced no effective results in eczema.

Death of Prof. Louis Ribadeau-Dumas.—France lost one of the best-known chiefs of one of its greatest schools of pediatrics and its first pediatrist, Louis Ribadeau-Dumas. He was a disciple of Legendre, Beclère, and Netter. He studied particularly parenteral infection and tuberculosis of infants. His works on renal function in infants are famous. At the last Pediatrics Congress, he was elected president for the next congress, taking place in Algiers in 1953. At the meeting of the 15th of June, 1951, of the Medical Society of the Paris Hospitals, the president, Prof. Robert Debré, emphasized the loss to the world and to French medicine through the death of this great master.

LONDON

Annual Representative Meeting of the British Medical Association.—The Annual Representative Meeting was held in the Great Hall of the B. M. A. House, London, June 13-16. Dr. J. A. Brown, a physician of Birmingham, was chairman. Dr. S. Wand was deputy chairman. Other officials on the platform were Dr. A. W. Sichel of Capetown, president-elect, Dr. E. A. Gregg, chairman of the council, Sir Henry Cohen, president, and Mr. A. M. A. Moore, treasurer.

Dr. Rowland Hill, chairman of the Central Consultants and Specialists' Committee, submitted the report for his committee. He paid tribute to the Joint Committee of Consultants (i. e., his committee and representatives of the Royal Colleges), on their work with the Minister of Health.

Dr. Barbara Abercromby, Liverpool, called attention to the fact that there are still many men of consultant status doing consultant work who have not yet after three years been given the status of consultant with the National Health Service. The Ministry of Health promised a review of their position, terms of service, and remuneration before the end of 1951, and she moved that, in fairness to the applicants, the majority of the members of the new committee to review their position should consist of persons who had not assessed their grading on previous occasions. Dr. A. Lawrence Abel, a surgeon and member of the council, of Marylebone, London, supporting the motion, said that he knew cases of senior men, well respected in the profession, who had been the only surgeon of a hospital or the senior surgeon of a big hospital, and had been for three years designated as "senior hospital medical officers" and not as consultants, simply because they were also general practitioners. The representative body had been given a promise that all senior hospital medical officers who wished to appeal would be regarded during 1951; this had not been done, and he did not think that it would be.

Dr. G. L. Barber, mid-Essex, moved that the strongest support should be given to the Joint Committee's representations to the Ministry with regard to the appointment of hospital consultants. Danger was not apparent in the machinery for their appointment, since the Ministry had made a regulation which allowed many lay members to adjudicate on the qualifications of a consultant.

A long and important statement was made. Dr. Wand, chairman of the General Medical Services Committee, discussed remuneration claims of family doctors under the National Health Service. He stated that a year ago we were engaged in an inquiry into the expenses of practices in order to arrive at a statement of the net incomes of doctors from the National Health Service. At that time the Minister agreed that for the present the Spens report should remain the basis of the remuneration of general medical practitioners. Dr. Wand pointed out that the Spens report had made its recommendations in net terms and at prewar values. The public does not realize that roughly 40% of a doctor's income goes toward expenses. Out of the annual capitation fee of approximately $2.40, the doctor earns less than 3 cents per week as net remuneration, and this is subject to tax, as is everybody else's remuneration, but his expenses have gone up very considerably, and, as the cost of living rises, so the net remuneration goes down. The Spens report recommended that a certain proportion of doctors should earn upward of $7,000 a year at prewar values. It recommended that there should be an incentive to go into general practice and that a doctor should have a reasonable life, so that he might give his best to the community, with ample opportunity for study and leisure.

The doctors' representatives met the Minister on February 28, and as a result received a letter indicating that there was a prima facie case for inquiry. In May, 1951, the result of the income tax inquiry into practice expenses was received. The two sides are still in dispute as to whether there should be a deduction from the gross income of 36.5% or 37.5% for practice expenses.

On May 9, a six-hour meeting with the Minister revealed three things. First, that the Chancellor of the Exchequer had placed a ceiling of 400 million pounds on the Health Service (i. e., $1,120,000,000). It will be remembered that the previous year's costs approached $1,400,000,000. Second, the Ministry was to effect a redistribution among the doctors of the total pool of monies. Third, the Ministry was anxious to secure a reduction in the bill for drugs. It was proposed that there should be a working party of the two sides of the details of these points.

To increase the family doctor remuneration, a sum of two million pounds ($5,600,000) was to be taken from general funds allotted to National Health. This sum represented approximately 11% of present practice expenses, that is, for the year ended March, 1950. Since that time there had been a general increase in costs. The Ministry has undertaken to hold a further inquiry and to bring the figures for expense estimates up to their 1951 level. This further inquiry would doubtless show that practice expenses were not far short of the two million pounds ($5,600,000) offered. If the practice expenses proved to be higher than this sum, family doctors would be actually worse off. This $5,600,000 represented a maximum offer by the Ministry.

It would appear, said Dr. Wand, that the government, having plunged into a comprehensive medical service against the advice of the profession, felt that the family doctors should be the people to carry the burden, and he could not see why the niggardly offer that had been made should be open to the interpretation that the family doctors' remuneration might depend on depriving the patient of necessary medicaments. Usually, he said, doctors were careful when they prescribed. There was disciplinary machinery in existence for dealing with those who were not. The doctors themselves took part in the machinery, and they saw that those who were unnecessarily extravagant in their prescribing had appropriate reductions made in their remuneration. The machinery had been set up a long while ago.

In regard to the committee's claim for more money to be devoted from the pool to the family doctor, the committee wished to take part in the settlement of this claim, because it would be in the public interest. It was difficult to set a precise figure for the amount of the claim: statements of receipts by doctors up to 1950 were available, but not statements of those receipts up to March, 1951. The number of doctors in March, 1950, was known, but not the number today, and the exact interpretation of the income tax figures for the year ended March, 1950, was still in dispute. The figure in dispute was 1%, but it was not known how much practice expenses had gone up since then.

In conclusion, Dr. Wand said that the committee was recommending that its claim should be put to arbitration and the arbitration must have regard for the change in the value of money since 1939.

ECUADOR

Pan-American Congress of Phthisiology.—The Ninth Pan-American Congress of Tuberculosis was held in Quito and Guayaquil, July 15 to 23, 1951. Dr. Jorge A. Higgins, president of the Latin-American Union of the Societies of Phthisiology and also president of the National Campaign Against Tuberculosis in Ecuador, was the president of the congress.

At the first plenary session, the delegates of Ecuador, Argentina, Bolivia, and Brazil dealt with the official topic: "Antibiotics in the Treatment of Tuberculosis." This was also the topic of the second session, when the delegates of Colombia, Chile, Cuba, and Mexico reported the results of their experiences, and of the third session, with reports from the delegates of Uruguay and Venezuela.

Experimental tuberculous superinfection was discussed in the fourth session by the Argentine delegates. At this session the following topics were presented: "Study of Contacts Based on Roentgenograms, Bronchial Lavage, and Bronchoscopy"; "Results of Ten Years' Experience in Application of the Law of Preventive Medicine in Tuberculosis," and "Evolution of Tuberculosis in a Community Regularly and Periodically Examined," "BCG Vaccination in Mexico," and "Study of Pulmonary Circulation in Tuberculosis."

At the fifth scientific session, the delegates from Uruguay dealt with the subject of mass examination in Uruguay. The following articles were read: "Dispensary for Detection of Foci: Its Prophylactic Role Within an Establishment for Tuberculous Patients," "Systematic Mass Examination Among Visitors and Patients Attending Clinics and Patients Hospitalized in Five Hospitals in Montevideo," and "Systematic Mass Examination Among the Patients of a Gynecologic Hospital." The delegates of Venezuela dealt with sanitary unity and the fight against tuberculosis. The delegates of Ecuador reported on treatment of pulmonary tuberculosis with paraaminosalicylic acid. Other subjects were aerosol therapy with paraaminosalicylic acid in pulmonary tuberculosis and treatment of tuberculosis with thiosemicarbazone.

Some of the conclusions reached by the congress in regard to chemotherapy of tuberculosis follow. Although antibiotics are valuable in the treatment of tuberculosis, the classic treatments do not lose their importance and indications. Streptomycin resistance, which appears during administration of variable amounts of the drug simultaneously with clinical signs of lack of therapeutic efficacy of the drug, is a fact to be considered in the course of determining the duration and indications of its use. The optimum dose is 1 gm., either daily or every two or three days. In diffuse acute forms and in tuberculous meningitis, daily doses from 1.50 to 2 gm., given with other antibiotics, are advisable. The use of streptomycin with other drugs, especially paraaminosalicylic acid, is advisable to prevent streptomycin resistance and to reinforce the therapeutic action of streptomycin. The route of administration, e. g., intrathecal, intrapleural, and aerosol, should be determined by the location of the disease. Hematogenous lesions and early exudative lesions, with or without cavities, have responded best to this therapy. Definite indications for streptomycin therapy are primary pulmonary, diffuse miliary, laryngeal, and meningeal tuberculosis and polyserositis.

In some extrapulmonary lesions, larger doses than the aforementioned ones may be administered; these should not interfere with the classic medicosurgical indications. The antibiotics should not be used indiscriminately in the course of collapse therapy. They should be used to attenuate the course of the lesions and to prevent and control complications of the operation. They have increased the indications for surgical operations and have often improved the prognosis. Amithiozone requires cautious use, and should be administered by specialists only, to prevent toxic effects and the allergic disturbances it usually elicits. Clinical experience is not sufficient to permit definite conclusions concerning its indications and results.

ARGENTINA

First Pan American Congress of Medical Education.—This Congress was held May 14-18, as part of the celebrations in honor of the 400th anniversary of the founding of the University of Lima, Peru. Representatives of all the American nations attended the meetings. The "Declaration of Lima on Medical Education" was drawn up; it was decided to establish a permanent Pan American Medical Education Bureau in Lima under the direction of Prof. Carlos F. Krumdieck. The next congress is to be held in São Paulo, Brazil, in January, 1954, on the occasion of the 400th anniversary of the founding of that city.

The most important recommendations by the congress were as follows: 1. Extension of studies in preventive and social medicine. 2. The professional degree should be a guarantee of a general knowledge in medicine, but specialization should be acquired after graduation. Research should be stimulated in postgraduate training. 3. Syllabuses must be arranged in three cycles; basic, clinical, and internship, with close interrelationship among them. 4. International cooperation.

Further recommendations were as follows: 1. Objective teaching and active seminars. 2. Compulsory internship. 3. Professorial chairs should be well equipped with the necessary apparatus for research and teaching. 4. Students should be selected, and only as many admitted as can be adequately dealt with. 5. Stimulation of scientific investigation among the professors. 6. At least one medical school with a high scientific standard should be organized in each country. 7. The organization and maintenance of schools of public health.

Thyroid Function and Endemic Goiter.—Endemic goiter is present in several Argentine provinces, along the Andes, in Misiones, and in certain central mountainous districts. Iodine deficiency in food, water, and air was studied by Dr. Pedro Mazzocco in the Institute of Physiology of the University of Buenos Aires, then under the directorship of Dr. Bernardo A. Houssay. Dr. J. T. Lewis in 1925 conducted a survey of the problem in some provinces and organized a system of prophylaxis with iodine which was not followed regularly. The use of iodized salt in those districts was recommended by Drs. Houssay, del Castillo, and Escudero but was not put into practice, despite several official regulations.

Dr. Héctor Perinetti, a well-known surgeon, was appointed director of the Goiter Institute, organized by the recently founded Faculty of Medicine in the University of Cuyo. He visited Prof. Means' service in Boston (Mass.) and, while there, suggested that a group from the Massachusetts General Hospital and Harvard University should study thyroid function by means of radioactive iodine in the city of Mendoza, which is in an endemic goiter district where there have been no measures for goiter control. This investigation was sponsored by the University of Cuyo, Harvard Medical School, and the Massachusetts General Hospital. The Rockefeller Foundation, the Loomis Foundation, Parke, Davis and Company, and the Armour Laboratories provided funds, equipment, and drugs. Radioactive iodine was supplied by the Oak Ridge Laboratory of the United States Atomic Energy Commission. The research workers who came to Argentina were Drs. J. B. Stanbury, D. S. Riggs, and G. L. Brownell, with Miss E. Brown as technician. They worked in cooperation with Drs. H. Perinetti and J. E. Itoiz of Mendoza, and Drs. E. B. del Castillo, E. Trucco, and A. B. Houssay Jr. of Buenos Aires. The investigations took seven weeks; 125 subjects were studied. Some important facts were demonstrated, particularly the great uptake of radioactive iodine by the thyroid gland in goitrous patients. This uptake is related to iodine deficiency and is inversely proportional to the amount of iodine excreted in the urine. These goiters were very sensitive to thyrotropic hormone, and a clinical survey showed hypothyroidism was exceptional.

This study was given great prominence in official newspapers, which praised the cooperation of the University of Cuyo, the government of Mendoza, and the Argentine National Commission of Atomic Energy.

V 14
1951

CORRESPONDENCE

SECOND ATTACKS OF POLIOMYELITIS

To the Editor:—To supplement and confirm Dr. Bissell's letter in the August 18 issue of THE JOURNAL, regarding second attacks of poliomyelitis, a detailed histopathological report of the central nervous system in his case will be found in a paper by Faber and Silverberg in the *Journal of Experimental Medicine* for April 1, 1946 (Vol. 83, pp. 339-340, case 8). We also recovered poliomyelitis virus from a sample of the cord.

The material had been submitted to us by Dr. Frederick Proescher of Santa Clara, who performed the autopsy. We regret that at the time we prepared our manuscript we had not been informed of Dr. Bissell's interest in the case, and for this reason failed to give him proper credit.

HAROLD K. FABER, M.D.
Dept. of Pediatrics, Stanford University
School of Medicine, San Francisco.

ESOPHAGEAL OBSTRUCTION DUE TO SERUTAN®

To the Editor:—In the July 21, 1951, issue of THE JOURNAL (page 1129) is a case report of esophageal obstruction due to serutan.® Inasmuch as many of my colleagues missed this article, I think it advisable to report another case.

B. A., 56, on Aug. 21, 1951, took a teaspoonful of serutan® granules, followed by a sip of water, and then another teaspoonful of granules, followed by a glass of water. There was an immediate sense of fulness and pain behind the sternum, and the water was regurgitated. All food and drink taken that day was regurgitated. At 7 p. m. he presented himself for diagnosis and treatment, which was no problem, since I had just finished reading the article in THE JOURNAL.

The patient was admitted to Mercy Hospital, where x-ray with a small amount of iodized oil showed complete obstruction at the junction of the middle and lower third of the esophagus. Dr. Clyde Chamberlin was asked to see the patient for esophagoscopy. A scope was passed, and after two hours of alternate suction and use of forceps the obstruction was removed. X-ray follow-up with barium showed a normal esophagus. Recovery was uneventful.

VERNON RODEN, M.D.
Central Ave. at Second St.
Hamilton, Ohio.

POSTGRADUATE COURSES

To the Editor:—There is no ready answer to the question of why there were 20,000 less persons in attendance at postgraduate courses during 1950-1951 than in the preceding year. My own experience may project one facet of the problem. The courses I attended from 1945 to 1949 left me unsatisfied. Not a single subject was covered in a timely postgraduate fashion. In fact, I felt as if I were being "talked down to" and that I was expected to remain bewildered at the omniscience of the lecturers.

Most of us out in the field who seek postgraduate guidance want reassurance that we need not approach all medical problems confronting us with the confusion of a third year medical student ordering all the available laboratory and x-ray work. We need guidance and reassurance that our therapeutic approaches to problems remain sound and that we are not subjecting our patients to the hazards of remedies and modalities in their experimental stage. We want the living patient as a diagnostic problem, as a medical management problem, and as a laboratory problem limited to the degree of our patients' capacity to pay. One such problem a morning is worth 15 hours of sitting about in an amphitheater listening to lectures.

We are being overlectured and "overarticled." State journals, national journals, proprietary review journals, and drug firm releases probably do impress us, but do they teach us anything?

We sometimes learn that a new remedy is 50% effective clinically. Let us see the patients. Let us see the other 50%. Thereby some of us may be able to evaluate the effect on the total patient of that remedy. For in private practice, selectivity and discrimination are the keystones to sound medical judgment.

The true postgraduate course must revolve about the living patient, his abnormal physiology as defined by physical examination and related laboratory evidence, and the optimal methodology in therapeutics needed to return the patient to a healthy status. Obviously, such courses must be under the immediate guidance of experts. The expert in the use of the stethoscope should supervise and illustrate the auscultatory findings wherever they may be; the radiologist should correlate what he sees; and the patient himself will teach us the limitations of both the stethoscope and the x-ray.

The cardiologist with the stethoscope is worth a hundred electrocardiograms. We in private practice deal with heart failure more frequently than many clinics do, and the behavior of our patient's heart under the stresses of a day's living define the management and the prognosis much more acutely than any heart tracing has ever done. Postgraduate courses in cardiology should be attuned to the man out in the field rather than to the man specializing in cardiology. Every subject in medicine should be organized on the level to which a practicing physician will be attracted.

I have limited myself to the problem of the man in general practice in internal medicine seeking postgraduate training. The general surgeon, the obstetrician, and others may have other views. It would be well to hear from them all.

LEON H. GOLDBERG, M.D.
Nyack, N. Y.

MULTIPLE SCLEROSIS

To the Editor:—Adenosine 5-phosphate (AMP, "my-B-den") has recently been made available for medical use. The development of a method by Albaum and Lipshitz (*Arch. Biochem.* **27**:102, 1950) for the determination of adenine nucleotides in blood and its application to human volunteers by Albaum and others (*J. Clin. Invest.* **30**:525, 1951) have suggested various therapeutic applications based on the important role that adenine nucleotides play in intracellular metabolic processes. Adenosine 5-phosphate (20 mg. intramuscularly) was found to increase the adenosine triphosphate (ATP) of blood by as much as 5 mg./100 ml. It was suspected that this effect might be mediated through the increased formation of coenzymes, flavine adenine nucleotides, and other active compounds of adenylic acid. This effect might be expected to occur in other cells of the body (e. g., nerve, muscle, and gland).

Multiple sclerosis is a disease of the central nervous system in which many nerve cells are reversibly damaged. This is indicated by the pattern of spontaneous remissions that complicate clinical evaluation of therapeutic agents. It has recently been shown by Jones and co-workers (*Ann. Int. Med.* **33**:831, 1950) that the pyruvate-lactate ratio in the plasma of patients with active multiple sclerosis is abnormal. The reaction lactate pyruvate requires coenzyme I as a co-factor.

Ten patients with multiple sclerosis have been treated with adenosine 5-phosphate and water-soluble vitamins. The duration of treatment has varied from 1 to 22 months. One patient had no change in status in two months. Two patients had no significant change in nine patient months. One patient had moderate but not very helpful improvement in 10 months. Five patients had marked to moderate improvement in 60 patient months (6 to 22 months). Improvement was noted within three days to six weeks in the patients who responded. One patient, under treatment for one month, begins to show improvement that cannot yet be evaluated. In the 10 patients treated for 82 patient months, no signs or symptoms of new neurological lesions were observed.

These observations, while provocative and worthy of further investigation, do not yet warrant general therapeutic use of adenosine 5-phosphate and water-soluble vitamins in patients with multiple sclerosis. They are, however, encouraging enough

to justify carefully controlled studies by which objective evaluation can be made and optimum conditions and dosage schedules determined. The mechanisms of the biological and therapeutic effects of muscle adenylic acid can only be elucidated by careful clinical and biochemical studies. Such studies have been planned and will soon be under way.

ARTHUR SHAPIRO, M.D.
30 Schermerhorn St.
Brooklyn 2.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Aggravation of Cancer by Steel Dust Inhalation as Compensable Injury.—The petitioner filed a claim under the Workmen's Compensation Act to recover compensation for the death of her husband. From an order denying the claim, which was affirmed by the trial court, the petitioner appealed to the Supreme Court of Arkansas.

The deceased worked for the Southern Lumber Company almost continuously from 1918 to 1942. In April of the latter year, he went to the hospital where he died a few weeks later. The deceased was employed by the company as a saw-filer and performed his work in a room on the second floor of the mill building. The filing of the saws caused small particles of emery dust to fill the air and, according to the undisputed testimony, the room was poorly ventilated and had no provisions for the removal of the emery dust, filings, and saw-dust. Directly below the filing room were large saws used in cutting lumber, and dust and fumes from this operation drifted upward through cracks in the floor into the filing room and contributed to the hazardous condition of the air. In the petitioner's claim, the nature of the accident was given as "inhaling emery and steel dust" and the cause of injury or death as "epitheliomateous cancer."

Epitheliomateous cancer, said the court, is listed as an occupational disease in the Workmen's Compensation Law of Arkansas. However, the epitheliomatous cancer referred to in this act is one caused by tar pitch, bitumen, mineral oil, or any of those products, and there is no showing that the deceased's cancer was caused by any of these substances. The question that naturally follows, said the Supreme Court, is: Was the cancer caused or aggravated by an injury resulting in death? There is no substantial evidence in the record to the effect that the cancer was not aggravated by an injury. One of the medical witnesses testified "Q. As I get it, in all of the opinions that you have expressed about it, you have indicated that you don't think that the exposure to the emery dust and to these fumes caused the cancer, but that they would accelerate a cancerous condition, aggravate it and make it worse? A. I said 'might' instead of 'would', Mr. Wilson. Q. You said 'might'. Well, that is an expression that doctors use, isn't it, when they mean it does do it in some cases? A. Yes, that is right." The effect of this testimony, said the court, is that the witness does not know what causes cancer, but that the exposure to emery dust and fumes might accelerate or aggravate a cancerous condition. Therefore, it necessarily follows that his testimony is not substantial evidence to the effect that emery dust, saw filings and saw-dust did not aggravate a cancer, which resulted in the death of the deceased. Another medical witness testified that it was the emery dust that caused the cancer by constant irritation, while still a third testified that the inhalation of any irritant would aggravate a cancerous condition. The deceased's cancer, said the court, probably developed a year or a year and a half before his death. The fact that it took the cancer about a year and a half to kill after it started, does not make it any less an accident.

It was said in a prior Arkansas case "As stated in some of the cases, it is no less an accident when a man suddenly breaks down than when there is a like mishap to the machine he is operating, nor is it a defense that a workman had some predisposing physical weakness, but for which he would not have broken down. If the employment was the cause of the collapse, in the sense that but for the work he was doing it would not have occurred when it did, the injury arises out of the employment."

A disputed claim under the Workmen's Compensation Law should be considered by giving the terms of the Act a liberal interpretation in favor of the claimant. The Supreme Court said that the conditions under which the deceased worked and the testimony of the medical witnesses, who testified that such conditions caused or aggravated the cancer, all considered together was substantial evidence to the effect that the constant inhalation of the emery dust and saw-dust caused an irritation in the lung which accidentally aggravated a cancerous condition, within the meaning of the Workmen's Compensation Law, and caused the death of the deceased. Accordingly the judgment of the trial court was reversed and the cause was remanded to the Workmen's Compensation Commission with directions to make an award in favor of the petitioner. *Scobey v. Southern Lumber Co., 238 S.W. (2d) 640 (Arkansas, 1951).*

Naturopathy: Right to Use Nutritional Foods.—This was a rehearing of a case involving the scope of practice of a naturopath by the Supreme Court of Arizona.

The former opinion in this case (229 P. (2d) 713) was abstracted in the *J. A. M. A.* **147:**686 (Oct. 13) 1951. The petition for rehearing raised the question of the right of naturopaths to use nutritional food substances. As a matter of common sense, said the Supreme Court, the members of the naturopathic profession in their practice of the healing art are not barred by the statutory definition from prescribing for their patients foods commonly used for nutritional purposes, as distinguished from drugs.—*Kuts-Cheraux et al. v. Wilson et al., 230 P. (2d) 512 (Arizona, 1951).*

MEDICAL MOTION PICTURES

Modern Technics for Initiating Blood Cultures: 16 mm., color, sound, showing time 14 minutes. Prepared with the assistance of Otto Tod Mallery, Jr., M.D., University of Michigan. Produced in 1951 for Becton, Dickinson & Company by Mervin LaRue, Chicago. Procurable on loan from Becton, Dickinson & Co., Rutherford, N. J.

This film demonstrates the use of the "vacutainer" culture tubes. It emphasizes their advantages as compared with the old methods of collecting blood with a syringe and transferring it openly into the containers with culture medium. The advantages are obvious, and there is no doubt that the opportunity for contamination has been much reduced. With this procedure, one must have available a large variety of vacuum-containing culture bottles with various culture mediums. Since some of them are used only rarely, the result will be an unavoidable increase of cost of the whole procedure. The "vacutainer" technique will have limited application in some methods of blood culturing. The film will be of interest mainly to those working in laboratories, to public health personnel, and to physicians who are drawing blood for blood cultures. The photography and narration are well done.

At Our House: 16 mm., black and white, sound, showing time 9 minutes. Sponsored by the Vermont State Department of Health. Produced in 1950 by and procurable on rental or purchase from Communication Materials Center, 413 West 117th St., New York 27.

This film depicts the experiences of a family with a multiphasic screening project. It shows the various tests being given and indicates how unsuspected disease or disability can be discovered. The results of the tests are kept confidential, and, in those instances in which there is need for diagnosis and treatment, this is done by the family physician. Medical societies interested in the multiphasic program would find this film worth while and informative. The photography and narration are satisfactory.

V 14
1951

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

64:119-254 (Aug.) 1951

Cutaneous Medicine in Medical Curriculum. U. J. Wile.—p. 119.
Incontinentia Pigmenti: Report of Five Cases and Review of Literature. R. G. Carney.—p. 126.
Psychocutaneous Aspects of Persistent Pruritus and Excessive Excoriation. P. F. Durham Seitz.—p. 136.
Effects of Podophyllum on Basal-Cell Epitheliomas. C. F. Sims and N. Pensky.—p. 142.
Squamous-Cell Epithelioma That Simulates Sarcoma. L. J. Underwood, H. Montgomery and A. C. Broders.—p. 149.
Pyogenic Infections of Skin: Etiologic Factor in Acute Glomerulonephritis of Children. J. L. Callaway and H. B. O'Rear.—p. 159.
Treatment of Vesiculoerosive Stomatitis with Aureomycin Troches. A. A. Fisher and M. Leider.—p. 164.
Penicillin in Treatment of Experimental Syphilis of Rabbits: VII. Penicillin "S-R" and Procaine Penicillin G in Peanut Oil with Aluminum Monostearate, Alone and in Combination with Oxophenarsine Hydrochloride (Mapharsen®) or Bismuth Subsalicylate. J. A. Kolmer.—p. 169.
Pigmented Purpuric Eruptions. S. J. Randall, R. R. Kierland and H. Montgomery.—p. 177.
Generalized Herpes Zoster, Encephalitis and Lymphatic Leukemia: Case Report. L. Frank.—p. 192.
Tinea Barbae of Kerion Type Produced by Trichophyton Purpureum: Report of Case. K. Loewenthal and R. L. Rein.—p. 194.
*Case of Pemphigus Treated with ACTH. A. Rubin.—p. 196.

Pemphigus Treated with Corticotropin.—The patient had an extensive erythematous, edematous, oozing, crusted eruption on the legs and arms. There was also a spreading, dry, red, scaling rash on the lower part of the back and on the abdomen. Treatment during the first several months had included poison ivy injections, oral administration of numerous antihistamine drugs, and application of lotions. Since the patient's occupation involved contact with nitric and sulfuric acids, with brass, chromium, cyanides, and hydrochloric acid, a diagnosis of occupational dermatitis was first considered when the author saw the patient on June 7, 1950. There was some improvement following oral administration of aureomycin and local treatment with aluminum acetate (Burow's) solution and an antipruritic lotion, but later new bullae continued to appear. The patient was hospitalized, and pemphigus was diagnosed. During the early part of hospitalization treatment consisted in the administration of aureomycin and penicillin and of tannic acid compresses, which seemed more efficacious than soaks with potassium permanganate, aluminum acetate, or boric acid solution. Treatment with corticotropin (ACTH) was started Aug. 29, 1950, 10 mg. being given every six hours. Most of the bullae disappeared within two days; the throat cleared; and the patient felt much improved. The injections were continued for five days. The patient left the hospital completely free from bullae. There were no side effects from the medication. When medication at home was reduced first to three and then to two injections of 10 mg. during 24 hours, several new bullae appeared, and there continued to be a few bullae on the legs. Later all lesions healed, and the patient returned to work on Oct. 16. On May 3, 1951, the patient was still free from symptoms.

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of five days. Three journals may be borrowed at a time. Periodicals are available from 1940 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

An asterisk (*) before a title indicates that the article is abstracted.

A.M.A. Arch. Internal Medicine, Chicago

88:135-270 (Aug.) 1951

Functional Anatomy of Porta-Systemic Communications. E. A. Edwards.—p. 137.
Q Fever in California: VII. Clinical Features in 180 Cases. W. H. Clark, E. H. Lennette, O. C. Railsback and M. S. Romer.—p. 155.
*Studies on Antibiotic Synergism and Antagonism: Interference of Aureomycin or Terramycin with Action of Penicillin in Infections in Mice. R. S. Speck, E. Jawetz and J. B. Gunnison.—p. 168.
Studies in Disorders of Muscle: VI. Is Progressive Muscular Dystrophy an Endocrine or Metabolic Disorder? F. H. Tyler and G. T. Perkoff.—p. 175.
*Clinical Study of Hereditary Interstitial Pyelonephritis. G. T. Perkoff, F. E. Stephens, D. A. Dolowitz and F. H. Tyler.—p. 191.
Effects of "Artisone" Acetate and Cortisone in Patients with Rheumatoid Arthritis. A. M. Lefkovits and H. J. Schupbach.—p. 201.
Anticoagulants in Coronary Thrombosis with Myocardial Infarction. D. A. Rytand.—p. 207.
Clinical Evaluation of Corticotrophin Therapy. I. N. Rosenberg, A. P. Cleroux, M. S. Raben and others.—p. 211.
*Penicillin Therapy of Asymptomatic Neurosyphilis: Spinal Fluid Cell Count as Guide to Therapeutic Response and Re-Treatment. W. T. Ford, R. H. Wiggall and J. H. Stokes.—p. 235.

Antibiotic Synergism and Antagonism.—In vitro studies of Klebsiella pneumoniae and beta hemolytic Streptococcus pyogenes demonstrated interference of aureomycin and terramycin with the bactericidal action of penicillin on these test organisms. The greatest antagonism was observed when moderately bacteriostatic concentrations of aureomycin or terramycin were added to rapidly bactericidal concentrations of penicillin. The range of interference observed with any of the three drugs and the differences among them are chiefly functions of their activity against the test organism. White mice were infected by intraperitoneal injection of diluted cultures of Streptococcus and Klebsiella and were treated with aureomycin or terramycin and penicillin. Terramycin and aureomycin also diminished the therapeutic effect of penicillin in experimental infections. While the antagonistic effect of aureomycin and terramycin resembled that previously reported for chloramphenicol, important quantitative differences were observed. Chloramphenicol in a wide range of concentrations interfered with penicillin in Streptococcus infections of mice, whereas aureomycin and terramycin had sharp peaks of maximum antagonism, below and above which their interference was less noticeable. The relatively narrow range of interfering concentrations of these two drugs in vivo suggests that in prolonged treatment there is less likelihood of antagonism. This was borne out by the difficulty encountered in demonstrating interference with aureomycin and terramycin in multiple dose schedules. Although there was lack of interference with multiple doses, there was no indication of either additive or synergistic effects of these drugs with penicillin. Aureomycin or terramycin interfere with the bactericidal and therapeutic effects of penicillin in infections with organisms that are susceptible to penicillin action. The antagonism is a function of the biologic activity of the interfering drug. If aureomycin is inactivated by prolonged heating, it loses both its antibiotic effect and its ability to antagonize penicillin. No evidence was discovered of any physical or chemical interaction between penicillin and aureomycin or terramycin. The experimental evidence does not permit any conclusions concerning the possible clinical importance of antibiotic antagonism of the type described by the authors.

Hereditary Interstitial Pyelonephritis.—The clinical manifestations and the genetic background of interstitial pyelonephritis was studied in a group of 232 descendants of a single person in four generations. Of 134 living members who were examined, 29 females and 15 males had renal disease with the characteristics of chronic interstitial pyelonephritis, which led to the death in uremia of seven male members. No female member of the group had fatal or progressive renal disease of the type manifested by these seven male members and by two living symptomatic male patients who showed the clinical findings of

severe progressive renal disease. The mechanism responsible for this remarkably high incidence of pyelonephritis in one group of related persons is not clear. The greatly increased severity of the disease in the male patients as compared with the female patients in this group, in contrast to the common occurrence of progressive renal insufficiency from interstitial pyelonephritis in women in the general population, remained unexplained. Clinical, laboratory, and genetic data support the hypothesis that the nephritis in this group is related to the transmission of an incompletely sex-linked dominant gene.

Penicillin Therapy of Asymptomatic Syphilis.—A total dose of not less than 4,800,000 units of aqueous penicillin G or 4,800,000 units of penicillin in oil and wax was given in not less than eight days to 112 patients with asymptomatic neurosyphilis. Activity of the disease in the nervous system was manifested by an elevated cell count of eight or more cells per cubic millimeter of spinal fluid in all patients prior to treatment. Of the 112 patients, 10 (about 8.9%) failed to attain a normal cell count at the end of six months after treatment or showed an initial response followed by a secondary rise later on. Eight of these 10 "penicillin failures" were detected during the first year of follow-up. They should be considered rather failures of a particular treatment schedule, inasmuch as six of the eight patients who were retreated showed an immediate, favorable response when retreated with 9,000,000 units of penicillin. Penicillin therapy appears to be superior to any other form of treatment in asymptomatic neurosyphilis, but the minimum dosage should not be less than 5,000,000, preferably 9,000,000 units, given over a period of 10 days. Notwithstanding the effectiveness of penicillin therapy, it is still essential to follow the effects of treatment on the spinal fluid by periodic checking of the cerebrospinal fluid cell count. Signs and symptoms of degenerative symptomatic neurosyphilis may appear in patients with minimal but undetected parenchymatous involvement at the time of treatment, despite a good response in the spinal fluid.

A.M.A. Arch. Otolaryngology, Chicago

54:1-114 (July) 1951

Life of Alfonso Corti. E. V. Ullman.—p. 1.
Laryngocele. J. J. O'Keefe.—p. 29.
Laryngeal Obstruction Due to Antibiotic Therapy. O. E. Anderson. —p. 34.
Functional Deafness. F. Harbert and J. Sataloff.—p. 38.
Transtympanic Injection of Anesthetics for Treatment of Ménière's Syndrome. M. S. Ersner, E. A. Spiegel and M. H. Alexander.—p. 43.
Osteoma of Maxillary Sinuses: Report of Case. M. Ćurković.—p. 53.

American Heart Journal, St. Louis

42:1-160 (July) 1951

Seventeen Cases of Left Intraventricular Block Without Increased Heart Size. A. F. Nyssens, A. van Bogaert and A. van Genabeek.—p. 1.
Electrocardiogram in Pregnancy and Puerperium. J. Zatuchni.—p. 11.
Complete Heart Block in Pregnant Women: Review of Literature. E. Evans and L. Pohlman.—p. 18.
Spatial Vectorcardiography: Myocardial Infarction. V. L. Scherlis and A. Grishman.—p. 24.
Aneurysms of Sinuses of Valsalva. G. R. Veaning.—p. 57.
*Congenital Pulmonary Stenosis Without Overriding Aorta: Clinical Study. Y. Larsson, E. Mannheimer, T. Möller and others.—p. 70.
Value of Esophageal Electrocardiogram in Elucidation of Postinfarction Intraventricular Block. H. B. Burchell and R. D. Pruitt.—p. 81.
Contribution of Augmented Unipolar Extremity Leads to Pattern of Left Ventricular Hypertrophy in Horizontal or Semihorizontal Electrocardiographic Position. N. E. Goulder and R. W. Kissane.—p. 88.
Patient with Functional Cardiovascular Disorders (Neurocirculatory Asthenia). W. J. Walker.—p. 97.
Procaine Amide: Its Effect on Auricular Arrhythmias. A. I. Schaffer, S. Blumenfeld, E. R. Pitman and J. H. Dix.—p. 115.
Effects of Dietary Cholesterol and Bile Salt in Golden Hamster. W. Marx, L. Marx and H. J. Deuel Jr.—p. 124.
Use of Adrenolytic Drug, Regitine, in Pheochromocytoma. L. T. Iseri, H. W. Henderson and J. W. Derr.—p. 129.
*Splenomegaly Associated with Rheumatic Heart Disease: Its Diagnostic Significance. W. L. Bennett and T. M. Durant.—p. 137.
New Method in Electrocardiographic Technique for Use in Patients with Somatic Tremor. N. Glaubach.—p. 142.

Congenital Pulmonary Stenosis Without Overriding Aorta.—Larsson and associates apply the term "isolated pulmonary stenosis" to types of congenital heart disease in which there are signs of pulmonary stenosis without an overriding aorta. Isolated pulmonary stenosis differs essentially from pulmonary stenosis in the tetralogy of Fallot. Because of the absence of a right-to-left shunt, the patient remains free from cyanosis and the development of the child is usually normal without limitation of the physical capacity. In a study of 218 cases of congenital cardiac malformations by means of cardiac catheterization the authors were able to diagnose isolated pulmonary stenosis in 30 cases, equally divided as to sex. None of these children or young adults were cyanotic, and they had no symptoms of cardiac disease, except that a few noted slight dyspnea on exertion. A loud systolic murmur over the pulmonary orifice was the main reason for examination. On cardiac catheterization a right ventricular hypertension could, as a rule, be established. In most cases where the pressure in the right ventricle was only moderately increased, the prognosis seemed to be good without treatment. In patients with marked right ventricular hypertension surgical treatment (valvulotomy according to Brock) should be considered.

Splenomegaly with Rheumatic Heart Disease.—The combined occurrence of prolonged fever and a palpably enlarged spleen in a patient with rheumatic heart disease is considered almost diagnostic of subacute bacterial endocarditis by most clinicians. The possibility that the fever could result from rheumatic activity and the splenomegaly result from chronic passive congestion is generally considered unlikely, since it is assumed that congestion seldom leads to sufficient enlargement of the spleen to render it palpable. While it is important to emphasize any dictum favoring the early diagnosis of a disease such as subacute bacterial endocarditis, the diagnosis should not be insisted on when no confirmatory evidence is obtained by blood cultures. The present study was carried out to determine the diagnostic value of splenomegaly in patients with rheumatic heart disease. In a thorough study of 80 patients with rheumatic heart disease, the spleen was found to be palpable in 18 instances. In two the splenomegaly was due to subacute bacterial endocarditis, in two to coexisting portal cirrhosis, and in one probably to tuberculous dissemination. In the remaining 13 cases (16%), no cause, other than congestive failure, was found to explain the splenic enlargement, and clinical evidence of congestive failure was minimal or absent in a few of these cases.

American Journal of Clinical Pathology, Baltimore

21:501-600 (June) 1951

Enzyme Studies on Human Blood: X. Relation of Fibrinogen Concentration to Beta Naphthol Reaction of Plasma. W. B. Smith, L. Rosenfeld and G. Y. Shinowara.—p. 501.
Chylomicrons of Blood: Resumé of Literature and Recommended Counting Procedure. J. M. Frailing and C. I. Owen.—p. 508.
Chemodectoma ("Nonchromaffin Paraganglioma") of Mediastinum: Report of Two Cases. D. K. Duncan and J. R. McDonald.—p. 515.
Complement-Fixation Test in Diagnosis of Lymphogranuloma Venereum. D. G. Wetherbee, R. J. Hilfer, B. Maspero and D. M. Kuhns.—p. 521.
Possible Role of Ferritin in Production of Shock in Hemochromatosis. H. E. Taylor.—p. 530.
Cytologic Changes of Oral Epithelium in Nutritional Deficiencies. R. Toaff and J. M. Bromberg.—p. 536.
Uniformity of Cell Counts in Smears of Bone Marrow Particles. R. S. Faden and R. Yalow.—p. 541.
Scleroma (Rhinoscleroma): Further Studies on Etiologic Agent. M. G. Levine.—p. 546.
Cytology of Bronchial Aspirates in Early Diagnosis of Bronchogenic Carcinoma: Experiences in Small General Hospital. J. G. K. Harvey and J. W. Hooker.—p. 550.
Late Recovery of Chlorinated Hydrocarbons (Carbon Tetrachloride) from Postmortem Tissue. D. M. Spain and A. Frey.—p. 558.
Preparation and Assay of Red Cell Fraction of Rh Factor. B. B. Carter. —p. 561.

American J. Digestive Diseases, Fort Wayne, Ind.

18:205-228 (July) 1951. **Partial Index**

Fulminating Trichiniasis. E. S. McCabe and J. Zatuchni.—p. 205.
Salmonellosis and Shigellosis in Cook County, Illinois: I. Classification of 600 Salmonella and Shigella Strains Isolated from Patients of Cook County Hospital. O. Felsenfeld, V. M. Young and T. Yoshimura. —p. 209.
Effect of Detergent Complex on Rate of Secretion of Gastric Juice and Its Components in Total Pouches of Stomach. O. E. Lobstein and S. J. Fogelson.—p. 213.
Effect of Detergent Complex on Deactivation and Rate of Reappearance of Lysozyme Activity in Gastric Juice Fractional Samples. O. E. Lobstein and S. J. Fogelson.—p. 214.
Importance of Liver in Dietary for Tuberculosis. J. Gershon-Cohen. —p. 215.
Effects of Vagotomy and Phrenicotomy on Cardia. N. C. Jefferson, C. W. Phillips, M. M. Proffitt and H. Necheles.—p. 217.

V 14
1951

American Journal of Hygiene, Baltimore

54:1-156 (July) 1951. **Partial Index**

Q Fever in California: V. Serologic Survey of Sheep, Goats and Cattle in Three Epidemiologic Categories, from Several Geographic Areas. E. H. Lennette, B. H. Dean, F. R. Abinanti and others.—p. 1.
Id.: VI. Description of Epidemic Occurring at Davis, California, in 1948. W. H. Clark, A. S. Bogucki, E. H. Lennette and others.—p. 15.
Id.: VIII. Epidemic of Q Fever in Small Rural Community in Northern California. W. H. Clark, M. S. Romer, M. A. Holmes and others. —p. 25.
Id.: IX. Outbreak Aboard Ship Transporting Goats. W. H. Clark, E. H. Lennette and M. S. Romer.—p. 35.
Id.: X. Recovery of Coxiella Burneti from Air of Premises Harboring Infected Goats. E. H. Lennette and H. H. Welsh.—p. 44.
*Combined Yellow Fever-Smallpox Vaccine for Cutaneous Application. R. G. Hahn.—p. 50.
Studies of Rickettsialpox: I. Recovery of Causative Agent from House Mice in Boston, Massachusetts. H. S. Fuller, E. S. Murray, J. C. Ayres and others.—p. 82.
Studies on Plasmodium Gallinaceum: I. Characteristics of Infection in Mosquito, Aedes Aegypti. D. E. Eyles.—p. 101.
Differentiation of Types of Poliomyelitis Viruses: IV. By Reciprocal Neutralization Tests. H. A. Howe.—p. 113.
Experimental Studies on Passive Immunization Against Poliomyelitis: I. Protection with Human Gamma Globulin Against Intramuscular Inoculation, and Combined Passive and Active Immunization. D. Bodian.—p. 132.
Effect of Available Residual Chlorine and Hydrogen-Ion Concentration upon Eyes of Swimmers. E. W. Mood, C. C. Clarke and A. Gelperin. —p. 144.

Combined Yellow Fever-Smallpox Vaccine for Cutaneous Application.—The preparation of a combined yellow fever-smallpox vaccine for cutaneous administration is described. The yellow fever component is the 17 D strain in chick embryo while the vaccinia virus is in phenolized sheep lymph, both being mixed with gum arabic to a total concentration of the latter of 15%. The mixture is then frozen and dried in a vacuum. The combined product is highly efficient for immunization against both diseases, withstands storage well, and may be produced and applied cheaply.

American Journal of Medicine, New York

11:1-132 (July) 1951

New Method of Equating and Presenting Bipolar and Unipolar Extremity Leads of Electrocardiogram: Advantages Gained in Visualization of Their Common Relationship to Electric Field of Heart. J. S. Graettinger, J. M. Packard and A. Graybiel.—p. 3.
Exercise Electrocardiogram: Aid in Diagnosis of Arteriosclerotic Heart Disease in Persons Exhibiting Abnormally Large Q3 Waves. C. F. Shaffer and D. W. Chapman.—p. 26.
Clinical and Cardiac Catheterization Studies in Four Cases of Eisenmenger's Complex. R. S. Cosby, D. C. Levinson, G. C. Griffith and others.—p. 31.
*Diagnosis of Masked Hyperthyroidism in Cardiac Patients with Auricular Fibrillation. M. M. Bortin, S. Silver and S. B. Yohalem.—p. 40.
*Treatment of Thyroid Carcinoma with Radioactive Iodine (I^{131}). A. S. Freedberg, A. L. Ureles, M. F. Lesses and S. L. Gargill.—p. 44.
Management of Carcinoma of Prostate: Study of Hormonal and Surgical Therapy in 100 Patients. J. H. Harrison and E. F. Poutasse.—p. 55.
Effects of Certain Antispasmodic Drugs on Intact Human Colon, with Special Reference to Banthine (β-Diethylaminoethyl Xanthene-9-Carboxylate Methobromide). F. Kern Jr., T. P. Almy and N. J. Stolk. —p. 67.
Canicola Fever: Review, with Report of Two New Cases. B. L. Rosenberg.—p. 75.

Masked Hyperthyroidism and Auricular Fibrillation.—Fifty-five patients with auricular fibrillation without overt hyperthyroidism were studied by radioiodine excretion and plasma protein-bound iodine determination. An excretion of less than 20% of a tracer dose of 100 μc of radioiodine with an adequate urinary output is considered diagnostic of hyperthyroidism. A value of 30% or more generally excludes the possibility of thyrotoxicosis. A value greater than 8 γ per cent of plasma protein-bound iodine is diagnostic of hyperthyroidism. The diagnosis of masked hyperthyroidism was established by these two methods in eight (15%) of the 55 patients studied. Patients with auricular fibrillation due to marked hyperthyroidism may be discovered by routine search using radioiodine excretion or plasma protein-bound iodine determination. The presence of thyrotoxicosis should be excluded in all patients with auricular fibrillation by use of these tests.

Radioactive Iodine in Thyroid Carcinoma.—Of 11 patients between 14 and 74 with carcinoma of the thyroid, six were treated with therapeutic doses of radioactive iodine (I^{131}). In one patient with papillary adenocarcinoma of the thyroid and a solitary metastasis to the lung, resolution of the pulmonary metastasis followed treatment with radioactive iodine. The therapeutic effect of radioactive iodine was considered worth while in two other cases, while in the remaining three cases no improvement was noted. Myxedema was induced in each of the six patients treated with radioactive iodine by one or more doses. It was allowed to persist for at least three months before desiccated thyroid was given in daily doses of 60 to 180 mg., which resulted in prompt relief of the symptoms of myxedema. In two patients thyroidectomy was attempted but was not feasible. In three others total thyroidectomy apparently had been accomplished previously. In each instance tracer studies showed uptakes in the thyroid gland region in the euthyroid range. The total therapeutic dose of radioactive iodine in each patient ranged from 20 to 209 mc.; the retention in the thyroid gland was 5 to 24 mc. No serious adverse effects of the iodine were observed. Transient thyroiditis and radiation sickness occurred in three of the six patients after therapeutic doses. A significant decrease in hemoglobin and red blood cell count was observed in one patient six months after he had received 108 mc. of I^{131}. Tracer studies were performed on the remaining five of the 11 patients. Following these studies total thyroidectomy was performed in two and hemithyroidectomy in three. Radioactive iodine distribution studies or radioautographs showed no evidence of increased uptake or localization of the iodine in the tumor tissue. Therapeutic doses were therefore not administered. Radioactive iodine is an important therapeutic agent in the treatment of selected instances of thyroid carcinoma.

American Journal of Obstetrics & Gynecology, St. Louis

62:1-240 (July) 1951. **Partial Index**

Clinicopathological Classification of Endometrial Carcinoma Based on Physical Findings, Anatomical Extent, and Histological Grade. W. F. Finn.—p. 1.
Advantages to Mother and Infant of Amphetamine in Obstetrical Analgesia. S. Abel, Z. B. Ball and S. C. Harris.—p. 15.
Premature Separation of Normally Implanted Placenta: Clinical Review of 340 Cases, Sloane Hospital for Women, 1933-1949. S. M. Bysshe. —p. 38.
Prolapse of Cord During Labor. A. N. Fenton and D. A. D'Esopo. —p. 52.
*Late Complications Following Irradiation of Pelvic Viscera. W. C. White and F. W. Finn.—p. 65.
Clinical Behavior of Granulosa-Cell Tumor of Ovary. W. G. French. —p. 75.
Endocrine Factors in Cancer of Cervix Uteri. H. E. Nieburgs.—p. 93.
Results of Experiment in Control of Pelvic Cancer. C. Macfarlane, M. C. Sturgis and F. S. Fetterman.—p. 102.
Abdominal Myomectomy, Advantages and Disadvantages. E. W. Munnell and F. W. Martin Jr.—p. 109.
Fetal Trauma from Forceps Delivery. T. S. Lloyd Jr., S. V. Ward and T. B. Sellers.—p. 129.
Use of Muscle-Relaxing Drugs in Complicated Deliveries. B. R. Austin and T. W. Mering.—p. 143.
Acute Appendicitis in the Obstetric Patient. H. D. Priddle and H. C. Hesseltine.—p. 150.
Carcinoma of Cervix in Jewish Women. A. Rothman, L. P. Rapoport and I. Davidsohn.—p. 160.
Transverse Diameter of Inlet. D. F. Kaltreider.—p. 163.
Relation of Leucoplakic Vulvitis to Squamous Carcinoma of Vulva. I. I. Langley, A. T. Hertig and G. V. S. Smith.—p. 167.

Complications of Irradiation of Pelvic Viscera.—The complications of radium or roentgen therapy employed for carcinoma of the uterus occur months to many years after irradiation. Cancer of the cervix is a lethal disease. Adequate doses of radium and roentgen rays are necessary to accomplish a cure. It is not possible to adequately screen off the surrounding tissue, so that some complications will inevitably develop. The authors discovered in their records only one clear-cut case of spontaneous fracture following pelvic irradiation. Other reports suggest that the incidence of spontaneous fractures is about 1% in those receiving intensive pelvic irradiation. In urinary tract injuries, late complications may come on suddenly. Symptoms are frequency, hematuria, and dysuria. Cystoscopy may show localized edema surrounding an indolent ulcer covered with gray slough. Surgery is rarely necessary. There is another group in which the onset is more insidious. The bladder symptoms are less severe, but the patient may have pain in the flank or upper quadrant, with chills and fever. Investigation reveals a stricture

147
951

of the ureter, with dilatation above and hydronephrosis or pyonephrosis. If this is recognized early enough, the kidney and ureter may be saved, and the patient relieved by dilatation of the stricture. Repeated urological studies should be made on patients who have undergone pelvic irradiation, so that treatment might be instituted before serious damage has been done. The incidence of damage to the intestine is difficult to estimate. There may be permanent damage to the rectum, sigmoid colon, and ileum, which manifests itself as thrombosis of the vessels, necrosis of the mucous membrane with fibrosis of the wall of the intestines, and secondary contracture of the ileum. The ulcerations may erode into large vessels, resulting in massive hemorrhage; or they may erode through the wall, so as to produce a perforation with peritonitis. Contracture alone may produce partial or complete obstruction. Although conservative therapy is possible, in many cases elective surgery is preferable.

American Journal of Occupational Therapy, Milwaukee

5:137-184 (July-Aug.) 1951

Need for Occupational Therapy in Retinal Detachments. G. Clark. —p. 137.
Occupational Therapy Program for Eye Patients. T. L. Wellerson.—p. 140.
Blindness and Functional Normality. C. G. Ritter.—p. 146.
Use of Educational Toys in Training of Blind Preschool Children. J. Brown.—p. 149.
Role of Dog Guide in Field of Rehabilitation. E. L. Hutchinson.—p. 153.
Independent Foot Travel for the Blind with Use of Cane. N. Griggs. —p. 156.
Work Testing for the Blind. A. L. Stevens.—p. 159.
Vocational Rehabilitation for the Blind in Puerto Rico. M. I. Ponton. —p. 162.

American Journal of Public Health, New York

41:769-906 (July) 1951. **Partial Index**

*Survey of Laboratory-Acquired Infections. S. E. Sulkin and R. M. Pike. —p. 769.
Hazard of Acquiring Tuberculosis in Laboratory. E. R. Long.—p. 782.
Hazard of Acquiring Virus and Rickettsial Diseases in Laboratory. J. E. Smadel.—p. 788.
Effect of Ultraviolet Light upon Absenteeism from Upper Respiratory Infections in New Haven Schools. A. Gelperin, M. A. Granoff and J. I. Linde.—p. 796.
Observations on In-Plant Feeding Programs in New Jersey. M. P. Zealand, M. Sena and O. Sussman.—p. 806.
Health Department Activities in Field of Chronic Diseases. E. M. Holmes Jr. and P. W. Bowden.—p. 812.
Quality of Medical Care: Methodology of Survey of Medical Groups Associated with Health Insurance Plan of New York. H. B. Makover. —p. 824.

Infections Acquired in Laboratories.—The report tabulates 1,342 infections acquired as a result of laboratory work in the United States, with deaths in 39 instances, a fatality rate of 3.0%. Approximately one-third of the infections have been recorded in the literature; the remainder were discovered by a questionnaire mailed to nearly 5,000 laboratories. The laboratory-acquired infections included 775 bacterial, 265 viral, 200 rickettsial, 39 parasitic, and 63 fungus infections. At least 69 different agents were involved, but brucellosis, tuberculosis, tularemia, typhoid, and streptococcic infections accounted for 72% of the bacterial infections and 31% of all infections. Coccidioides outnumbers all other fungi as a cause of laboratory infection, owing undoubtedly to the highly infective nature of the chlamydospores. Laboratory infections with this agent are known to have occurred even in personnel not working directly with the fungus. Trained scientific personnel were involved in 1,015 of the infections; the remainder occurred in students, animal caretakers, janitors, and others. Research accounted for 308 cases, diagnostic work for 455, production of biologics for 25, and classwork for 29, while in the remaining cases a combination of activities was involved. The probable source of infection was indicated in all except 248 cases. The handling of clinical specimens and infected animals or ectoparasites accounted for 175 and 139 cases, respectively. There were 98 infections acquired in the autopsy room. Accidents, excluding autopsy accidents, were involved in 215 instances. The largest number of infections was associated with the use of a hypodermic needle and syringe.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

35:301-404 (July) 1951

Cerebral Blood Flow and Metabolism in Neurosyphilis: Effects of Penicillin, Induced Fever, and Other Therapeutic Measures. A. Heyman, J. L. Patterson Jr., F. T. Nichols Jr. and R. W. Jones.—p. 301.
Problem of Jarisch-Herxheimer Reaction in Penicillin Therapy of Cardiovascular Syphilis. H. A. Sinclaire and B. Webster.—p. 312.
*Treatment of Cardiovascular Syphilis with Penicillin. C. E. Wheeler and A. C. Curtis.—p. 319.
Syphilitic Paroxysmal Cold Hemoglobinuria Causing Transfusion Reaction: Response to Penicillin. N. P. Hill.—p. 329.
*Congenital Syphilis in One of Apparently Identical Twins. R. A. Raskin. —p. 334.
Recent Advances in Serodiagnosis of Syphilis. V. A. Puccinelli.—p. 340.
Quantitative Spinal Fluid Protein Determination: Comparative Study. B. A. Gross.—p. 350.
Eradication of Gonorrhea in District of Greenland. P. V. Marcussen and J. Rendal.—p. 356.
Investigation of Cultivation of Pleuropneumonia-Like Organisms from Man. H. E. Morton, P. F. Smith and P. R. Leberman.—p. 361.
Treatment of Early Lymphogranuloma Venereum with Aureomycin. I. L. Schamberg, O. M. Carrozzino and W. P. Boger.—p. 370.
Granuloma Inguinale: Further Observations on Results of Treatment with Aureomycin and Chloramphenicol. R. C. V. Robinson and B. Cronk.—p. 378.
Antibiotics Versus Donovania Granulomatis. C. H. Chen, R. B. Dienst and R. B. Greenblatt.—p. 383.

Penicillin in Cardiovascular Syphilis.—Although over six years have passed since penicillin was first used in the treatment of syphilis, its effect on cardiovascular involvement has not been so far established. Adverse effects might be expected in the form of the Jarisch-Herxheimer reaction and the therapeutic paradox. The literature on the use of penicillin in cardiovascular syphilis indicates that of about 190 cases, 155 patients had aneurysm, aortic insufficiency, or both, and 35 had diagnoses of uncomplicated aortitis. Since the latter diagnosis involves the possibility of error these patients are disregarded. The remaining 155 patients had evidence of either aneurysm or aortic insufficiency, or both. Approximately 130 patients of this latter group were given varying amounts of iodide and metal therapy before penicillin administration, while 25 had received only penicillin. There was no instance of an adverse reaction to penicillin. The authors report 21 patients who were previously untreated or who had received grossly inadequate treatment many years before. Clinical data on these 21 patients include age, duration of syphilis, cardiovascular symptoms, nature of the cardiac lesion, previous treatment, penicillin schedule, and cardiovascular follow-up. There was no evidence of an adverse effect of the penicillin treatment in the form of the Herxheimer reaction or the therapeutic paradox. Present indications are therefore that it is safe to treat cardiovascular syphilis with penicillin without first administering iodides or bismuth.

Congenital Syphilis in One of Identical Twins.—The mother of twins had no symptoms of syphilis, but a routine serologic test on July 7, at the time of her registration in the obstetric clinic, was positive. Labor began before antisyphilitic treatment was started, and male twins were delivered on Aug. 4. The placenta was not thoroughly examined to ascertain whether the twins were monovular or binovular, but they were apparently identical. The twins showed no evidence of syphilis and were not treated. Their blood and long bones were examined every week. Twin A was given a blood transfusion for signs of anemia. Later he showed signs of jaundice. Since the interval between transfusion and jaundice was only four weeks, the diagnosis of homologous serum jaundice was not considered, especially since the serologic test was now strongly positive for syphilis. A duplicate specimen of blood revealed a 4+ Kolmer reaction with a titer of 1:160. X-ray examination also revealed extensive periosteal changes and areas of destruction in the metaphysial ends of the long bones. Spinal fluid Wassermann test and colloidal gold test were also positive. That twin A had been transfused four weeks prior to the appearance of syphilis raised the question of transfusion syphilis, but Kahn, Mazzini, and Wassermann reactions were negative in the sample of blood. Furthermore, a patient who received the remainder of the same blood had a negative Wassermann reaction six months after the transfusion. The pathogenesis of the syphilis must remain speculative. It is conceivable that a localized area of the placenta was in-

V 14
1951

fected with spirochetes, and prior to or during parturition these spirochetes found their way into the umbilical vein of the infected twin. It is also possible that this twin was infected during delivery. There is the remote possibility that the other twin may also have been infected, but to a lesser degree.

Annals of Internal Medicine, Lancaster, Pa.

35:1-306 (July) 1951

Destiny of American College of Physicians. W. S. Middleton.—p. 1.
*Observations on Results of Subtotal Adrenalectomy in Treatment of Severe, Otherwise Intractable Hypertension and Their Bearing on Mechanism by Which Hypertension is Maintained. C. C. Wolferth, W. A. Jeffers, F. D. W. Lukens and others.—p. 8.
Effects of Priscol (2-Benzyl-4, 5-Imidazoline Hydrochloride) in Treatment of Peripheral Vascular Diseases. N. Frank, J. A. Strazza Jr. and J. T. Helsper.—p. 19.
Lack of Correlation Between Symptoms and Degree of Renal Impairment. L. H. Newburgh and A. A. Camara.—p. 39.
*Bacterial Endocarditis: Clinico-Pathologic Studies of Untreated, Treated and Cured Patients. H. L. Correll, J. M. Lubitz and M. C. F. Lindert.—p. 45.
Leukemia and Pregnancy: Report of Four Cases and Review of Literature. W. A. Sientz.—p. 59.
Clinical Study of Malnutrition in Japanese Prisoners of War. M. A. Schnitker, P. E. Mattman and T. L. Bliss.—p. 69.
Pulmonary Moniliasis. R. W. Oblath, D. H. Donath, H. G. Johnstone and W. J. Kerr.—p. 97.
Vasopressor Components of Pheochromocytomas. K. H. Beyer, C. A. Ross, V. D. Wiebelhaus and others.—p. 117.
Association of Graves' Disease with Myasthenia Gravis, with Report of Five Cases. G. Levy, W. R. Meadows and R. M. Gunnar.—p. 134.
Renal Anoxia Syndrome: Review and Report of 22 Cases. P. Gaberman, D. H. Atlas, E. M. Kammerling and others.—p. 148.
Studies in Disorders of Muscle: IV. Clinical Manifestations and Inheritance of Childhood Progressive Muscular Dystrophy. F. H. Tyler and F. E. Stephens.—p. 169.
Atypical Facial Neuralgia in Hypothyroid State. F. B. Watts.—p. 186.
Myelocytic Leukemia: Analysis of Incidence, Distribution and Fatality, 1910-1948. M. B. Shimkin, S. R. Mettier and H. R. Bierman.—p. 194.

Subtotal Adrenalectomy for Severe Hypertension.—In 16 patients one adrenal gland was removed during the second stage of thoracolumbar sympathectomy. The results, contrary to those previously reported by other workers, did not appear to be superior to those anticipated from thoracolumbar sympathectomy alone. The next step included more radical excision of adrenal tissue, ranging in 23 patients from removal of approximately 90% of adrenal tissue to complete adrenalectomy. In 15 patients the operation was limited to adrenalectomy and in eight it was combined with either limited or extensive sympathectomy. Of these 23 patients, 19 survived the operation and were followed up from one month to one year. The arterial blood pressure has been reduced in some patients from extremely high levels to a normal range by subtotal adrenalectomy alone with marked symptomatic improvement, relief from heart failure, improvement in renal plasma flow, and reduction in cerebral vascular tension. In order to achieve such results, it was necessary to remove more than 90% of adrenal tissue and create a degree of adrenal cortical insufficiency requiring at least minimal replacement therapy. The combination of subtotal adrenalectomy and sympathectomy has yielded more promising results than adrenalectomy alone. In one patient in the original group of 16 patients subjected to bilateral thoracolumbar sympathectomy and unilateral adrenalectomy in whom that operation had failed to control severe hypertension, the blood pressure has been maintained in a low normal range for over a year following another operation, in which approximately 90% of the remaining adrenal gland was removed. In five of six patients in whom removal of at least 95% of the adrenal tissue was combined with bilateral splanchnicectomy and bilateral removal of the paravertebral ganglions from the 12th thoracic to the 2nd lumbar inclusive, the early postoperative drop in pressure has tended to be more satisfactory than that obtained from adrenalectomy alone. If combined subtotal adrenalectomy and sympathectomy prove to be the most effective surgical attack on hypertension, its most effective control by nonsurgical methods may be directed both toward control of sympathetic nervous system activity and depression of adrenal cortical function.

Bacterial Endocarditis.—The clinical course was studied in 70 patients with bacterial endocarditis. Twenty-three were symptomatically treated; 11 were given sulfonamides; and 36 received antibiotics. Tissues were studied post mortem in 48 of these patients. Of the symptomatically treated patients all died, while of the patients treated with antibiotics and representing 42 infections or reinfections only 16 (44.4%) died within three months of termination of therapy. This change in the immediate mortality rate of bacterial endocarditis brought about by antibiotic therapy was due to early healing of the vegetations, with resultant decrease in the fatal embolic complications, and the institution of treatment before the development of myocarditis associated with heart failure. Halting the surface growth of the bacterial colonies allowed time for the vegetation to become adequately organized, thus inhibiting embolism, which caused the death of 11 symptomatically treated patients (47%). Occasionally, heart failure developed as a result of valvular destruction alone, but usually it was also associated with myocarditis, which developed because of delay in diagnosis and treatment. If the patient had symptoms for several months, myocarditis was almost invariably present in association with heart failure, which was usually fatal. For these reasons a delay in treatment seriously affected the prognosis for immediate cure. The age of the patient at the time of the infection was important. The mortality rate steadily increased beyond the age of 30. Correction for the distribution of population by decades revealed the incidence of the disease from 30 to 60 to be remarkably constant. When heart failure developed during the active phase of the disease, the immediate mortality rate was significantly increased. Subsequent pronounced cardiac disability developed in approximately one-third of those cured of the infection. Death within two years from heart failure occurred in approximately one-fifth of the patients. The late morbidity and mortality rates in adequately treated patients were caused almost entirely by heart failure. Increasing valvular deformity, particularly of the aortic valve, was of prime importance, whereas myocardial fibrosis due to the residuals of myocarditis was of undetermined but lesser significance. To improve these morbidity and mortality figures it will be necessary (1) to prevent the bacterial infection by recognition and treatment of the common predisposing factors, such as sore throat and dental extraction, and (2) to recognize and treat the disease before fatal embolism or heart failure occurs.

Cancer Research, Chicago

11:481-564 (July) 1951. **Partial Index**

Effect of Pyridoxine and Desoxypyridoxine on Rat Fibrosarcoma Grafts. J. B. Loefer.—p. 481.
Nuclei from Normal and Leukemic Mouse Spleen: II. Nucleic Acid Content of Normal and Leukemic Nuclei. M. L. Petermann and R. M. Schneider.—p. 485.
Tracer Studies on Metabolism of Gardner Lymphosarcoma: I. Uptake of Radioactive Glycine into Tumor Protein. E. Farber, S. Kitt and D. M. Greenberg.—p. 490.
*Experimental Studies on Etiology of Hodgkin's Disease. W. L. Bostick and L. Hanna.—p. 505.
Metabolic Degradation in Mouse of 1,2,5,6-Dibenzanthracene-9,10-C^{14}: II. 5-Hydroxy-1,2-Naphthalic Acid, New Metabolite. C. Heidelberger and W. G. Wiest.—p. 511.
Folic Acid Analogs and Growth of Embryo and Tumor Tissue. A. Taylor and N. Carmichael.—p. 519.
Intracellular Distribution of Protein, Nucleic Acids, and Riboflavin in Livers of Mice and Hamsters Fed 4-Dimethylaminoazobenzene. J. M. Price, J. A. Miller and E. C. Miller.—p. 523.
Transplantation of Tumors to Brains of Heterologous Species. H. S. N. Greene.—p. 529.
Neoplasms in Rats Treated with Pituitary Growth Hormone: V. Absence of Neoplasms in Hypophysectomized Rats. H. D. Moon, M. E. Simpson, Choh Hao Li and H. M. Evans.—p. 535.
Heterologous Growth and Passages of Mouse Sarcomas in Hamsters (Mesocricetus Auratus). J. Patti and J. J. Biesele.—p. 540.
Specificity of Hypervolemia and Congestive Changes in Tumor-Bearing Mice. J. Furth and J. Moshman.—p. 543.
Method for Determining Mutation Rate and Tumor Incidence Simultaneously. W. J. Burdette.—p. 552.
Effect of Visible Light on Development in Mice of Skin Tumors and Leukemia Induced by Carcinogens. J. J. Morton, G. B. Mider, E. M. Luce-Clausen and E. B. Mahoney.—p. 559.

Etiology of Hodgkin's Disease.—Hodgkin's disease has been looked on as a type of malignancy different from most of the other cancerous processes. Many of its characteristics suggest an inflammatory background. The possible infectious charac-

teristics of Hodgkin's disease have been reexamined by the previously unused technique of serial passage of the Hodgkin's disease lymph node extracts in embryonated chicken eggs. A slight lethal effect in the embryos was noted. The amniotic fluid was shown to inhibit the growth of Lee influenza virus grown in other chicken eggs. It showed no tendency to agglutinate the erythrocytes of the many animals tested or to sensitize the erythrocytes to known hemagglutinating viruses. The amniotic fluid had no untoward effect on animal inoculation via many routes. Precipitin and flocculation tests were uninformative, and complement fixation procedures showed some trends that deserve further study. The amniotic fluid collected after numerous serial passages from Hodgkin's disease-inoculated embryos has certain filterable, transferable, and virus-like properties. This material is now being studied by electron microscope, ultracentrifuge, and differential precipitation techniques.

Delaware State Medical Journal, Wilmington

23:165-192 (July) 1951

Hemolytic Anemia in Infectious Mononucleosis: Case Report. P. W. Huntington Jr.—p. 165.
Application of Bleeding and Coagulation Studies in Hospital. A. D. Richman and W. J. Hoopes.—p. 167.
Survey of Transfusion Reactions 1949-1950. Chow Ching Te and J. W. Howard.—p. 170.
Contact Dermatitis. A. D. King.—p. 173.
Common Virus Diseases of Skin. L. Katzenstein.—p. 175.
Glaucoma—Its Present Concept. A. W. Howland.—p. 180.
Dimethylane in Treatment of Dysmenorrhea. G. J. Boines and S. Horoschak.—p. 183.

Journal of Experimental Medicine, New York

94:1-86 (July) 1951

Histogenesis of Sebaceous Gland Carcinomas Produced in Rats by 2-Acetylaminofluorene. S. C. Skoryna, R. C. Ross and L. A. Rudis.—p. 1.
Observations by Electron Microscopy on Contraction of Skeletal Myofibrils Induced with Adenosinetriphosphate. C. A. Ashley, K. R. Porter, D. E. Philpott and G. M. Hass.—p. 9.
Localization of Adrenocorticotropic Hormone by Histochemical and Immunochemical Methods. J. M. Marshall Jr.—p. 21.
Sorption of Influenza Virus by Chicken Erythrocytes. T. P. Magill.—p. 31.
Passage of Coxsackie Virus (Connecticut-5 Strain) in Adult Mice with Production of Pancreatic Disease. A. M. Pappenheimer, L. J. Kunz and S. Richardson.—p. 45.
Sparing Effect of Coxsackie Virus Infection on Experimental Poliomyelitis. G. Dalldorf.—p. 65.
Influence of Physiological Blood Clotting Process on Coagulation of Blood by Staphylocoagulase. M. Tager and A. L. Lodge.—p. 73.

Journal of International College of Surgeons, Chicago

16:141-264 (Aug.) 1951

Primary Carcinoma of Ureter. H. M. Soloway.—p. 141.
Primary Carcinoma of Ureter. J. A. Bowen and L. Atherton.—p. 160.
Rhinoplastic Problems Confronting Rhinologist. M. S. Ersner, M. H. Alexander and D. Myers.—p. 165.
Fractures of Forearm. W. Johnson, R. G. Hickerson, B. E. Malstrom and E. G. Behrents.—p. 175.
*Stellate Ganglion Block in Treatment of Acute Subdeltoid Bursitis. E. J. Gordon.—p. 185.
Surgical Treatment of Abdominal Ascites Due to Cirrhosis of Liver: Preliminary Experience with New Cannula Button in Peritoneosaphenous Anastomosis. C. F. Schnee.—p. 199.
Simplified Photography for Surgeon. J. T. Lloyd.—p. 208.
Automatic Surgical Photographer. A. L. Soresi.—p. 213.
Roentgen Irradiation of Adrenal Glands: Results of Indirect Hormonal Research. M. A. Manzanilla Jr.—p. 222.
Drainage of Infected Peritoneal Cavity. A. P. Randazzo and E. Dul.—p. 231.

Stellate Ganglion Block in Acute Subdeltoid Bursitis.—The use of stellate ganglion block for subdeltoid or subacromial bursitis and other painful conditions was reported in 1945 and 1946. Gordon describes the results obtained with stellate ganglion block in 36 cases of acute subdeltoid bursitis. He used a 2% solution of procaine hydrochloride (in some patients 0.15% tetracaine [pontocaine®] hydrochloride was added for a prolonged blocking effect). It was thought that if the immediate effect of procaine were combined with the sustained (four to five hours) effect of tetracaine the number of injections required could be diminished, but little difference was noted in the final results. In most cases ¾ grain (48 mg.) of pentobarbital (nembutal®) or secobarbital (seconal®) was given 45 minutes before injection in order to reduce anxiety. At first, two or three blocks were given at intervals of one to three days, then one block was given at 24 hour intervals for a total of three blocks. Only rarely has a fourth block been required. The anterolateral approach of Murphey gave consistently good results and is recommended for maximum vasomotor effect in the upper extremity. There were no serious complications. Minor complications, such as transitory pain, temporary paresis of the upper extremity from extension of the anesthesia to the lower brachial plexus, and an intensely nervous and hysterical type of reaction, subsiding within a few minutes, were occasionally observed. Excellent results were obtained in 32 patients; only four did not have complete relief of all symptoms within seven days of the beginning of stellate block therapy. In these a few physical therapy treatments, such as diathermy or infrared, massage, and stretching exercises completely alleviated all symptoms within an additional two-week period. There were mild recurrences in two patients, after 7 and 12 months respectively, but both promptly responded to physical therapy. The calcium deposits were found to be absorbed in 16 of 18 patients who were examined roentgenologically from 6 to 18 months later. Discomfort, pain, disability, and economic loss are materially diminished by this treatment as compared with other forms of therapy.

Journal-Lancet, Minneapolis

71:257-296 (July) 1951

Practice of Medicine in Sweden. E. J. Tanquist.—p. 257.
Urinary Extravasation. S. S. Beirstein and M. J. Feeney.—p. 261.
Clinical Experience with New Analgesic Agent. C. L. Junkerman, R. C. Heen and H. W. Pohle.—p. 263.
Applying Psychiatric Principles in Medical Practice. P. C. Benton.—p. 266.
Hepatoma in Infancy: Case Report. R. B. Cochran.—p. 269.
3-0-Toloxy 1,2-Propanediol in Treatment of Rheumatic Diseases. I. F. Hermann and R. T. Smith.—p. 271.

Journal of Nervous and Mental Disease, New York

114:1-94 (July) 1951

Autonomic Changes Paralleling Psychologic Changes in Mentally Ill Patients. D. H. Funkenstein, M. Greenblatt and H. C. Solomon.—p. 1.
*Heroin Addiction in Adolescent Boys. P. Zimmering, J. Toolan, R. Safrin and S. B. Wortis.—p. 19.
Primary Pontile Hemorrhage: With Particular Reference to Respiratory Failure. A. T. Steegmann.—p. 35.
Recognition and Acceptance of Mood in Music by Psychotic Patients. B. Simon, J. D. Holzberg, S. L. Alessi and D. A. Garrity.—p. 66.

Heroin Addiction in Adolescent Boys.—For the past years there has been evidence of increasing drug addiction among the adolescents in the Harlem area of New York. During the first two months of this year, 65 boys and 19 girls were admitted to Bellevue Hospital with heroin (diacetylmorphine) addiction. The present report is based on the study of 22 boys, ranging in age from 14 to 17 years, who were hospitalized for heroin addiction. All but one were either Negroes or of Puerto Rican descent. Among pertinent social factors in the addiction is the feeling in these groups that they live in an alien, hostile culture that considers their racial characteristics as stamps of inferiority. They suffer almost continuous injuries to their self-esteem. The following character traits predominate in the group: lack of aggression, strong attachment to the mother, poor object relationships, omnipotent striving, and a tendency to regress. The management of this group is essentially a social-psychological and police problem. The authors suggest removal of the youthful addict to institutions for "normal" boys for periods up to two or three years with periodic trials at home.

Journal of Neurophysiology, Springfield, Ill.

14:257-336 (July) 1951. **Partial Index**

Observations on Physiological Action of Strychnine. P. D. Wall and N. H. Horwitz.—p. 257.
Experimentally Derived Correlates Between ECG and Steady Cortical Potential. S. Goldring and J. L. O'Leary.—p. 275.
Vasomotor, Cellular and Functional Changes Produced in Kidney by Brain Stimulation. E. C. Hoff, J. F. Kell Jr., N. Hastings and others.—p. 317.

V 14
1951

J. Pharmacology & Exper. Therap., Baltimore

102:145-214 (July) 1951. **Partial Index**

Metabolism of C^{14} Carboxyl Salicylic Acid in Dog and in Man. E. L. Alpen, H. G. Mandel, V. W. Rodwell and P. K. Smith.—p. 150.
Heparin-Like Activity of New Anticoagulant, Treburon. C. N. Mangieri, R. Engelberg and L. O. Randall.—p. 156.
Studies on Mechanism of Acute Beryllium Poisoning. K. W. Cochran, M. M. Zerwic and K. P. DuBois.—p. 165.
Antibiotic Lactones and Synthetic Analogs: III. Efficacy in Experimental Trypanosomiasis. N. J. Giarman.—p. 185.
Tetraethylammonium and Cholinesterase Activity. C. J. Kensler and R. W. Elsner.—p. 196.
Influence of Procaine and Some Related Compounds upon Experimental Auricular Flutter in Dog. B. B. Brown and G. H. Acheson.—p. 200.

Kansas Medical Society Journal, Topeka

52:313-360 (July) 1951

Bronchial Asthma from Therapeutic Point of View. J. K. Fulton.—p. 313.
*Encephalitis in the Midwest: I. Review of the Problem. T. A. Cockburn, E. R. Price and J. A. Rowe.—p. 316.
Handling of Casualties. W. L. Wilson.—p. 319.
Urology and Internal Medicine. H. L. Kretschmer.—p. 325.

Encephalitis in the Midwest.—Western equine encephalomyelitis and St. Louis encephalitis are arthropod-borne encephalitides that have been reported from the Missouri River basin. Epidemics of St. Louis encephalitis occurred in 1933 and 1937 in the city and county of St. Louis, Missouri, and western equine encephalomyelitis occurred in 1941 in North and South Dakota, Minnesota, and Nebraska. The equine epizootics (such as the "Kansas-Nebraska horse plague" in 1912 and those of 1937 and 1938, extending over the whole midwest) involved vast numbers of animals. Other viruses present that can produce the symptoms of encephalitis in man include lymphocytic choriomeningitis, poliomyelitis, herpes, and mumps. The diagnosis of encephalitis is difficult. The specific infections cannot be identified without complicated laboratory tests undertaken either to isolate the causal virus or to demonstrate a rising titer of antibodies. Few laboratories in the midwest are equipped to perform diagnostic work on encephalitis. In 1948 studies on the encephalitis problem in the midwest were begun by the Encephalitis Investigations Unit of the Office of Midwestern Communicable Disease Center Services, Kansas City, Kan. The objective of these studies is the clarification of the epidemiologies of the arthropod-borne virus encephalitides in the hope that some practical means of dealing with them may be found. There is no specific treatment, any available medication being for symptomatic relief only, so that the management is largely a matter of careful nursing. The death rate in epidemics of western equine encephalomyelitis and St. Louis encephalitis appears to be between 5 and 20%, and a number of patients who survive have residual paralyses or personality changes. There is no satisfactory method of prevention, although preventive inoculation is available for persons exposed to undue risk, and antimosquito precautions are advisable under certain circumstances.

Missouri State Medical Assn. Journal, St. Louis

48:493-596 (July) 1951

Surgery: Practical Solution of Inguinal Hernia Problem of Infancy and Childhood. C. J. Heifetz.—p. 509.
Psychiatric Screening of Medical Patients. C. F. Barritt.—p. 514.
Mesenteric Vascular Occlusion: Recovery of Case of Venous Occlusion. J. W. Fleming Jr.—p. 531.
Bleeding Meckel's Diverticulum. J. A. Nigro.—p. 534.

New England Journal of Medicine, Boston

245:39-82 (July 12) 1951

Nutritional Surveys of Population Groups. H. M. Sinclair.—p. 39.
*Comparison of Blood-Sugar and Urine-Sugar Determinations for Detection of Diabetes. D. Harting and B. Glenn.—p. 48.
Relation of Sex, Pregnancy and Menstruation to Susceptibility in Poliomyelitis. L. Weinstein, W. L. Aycock and R. F. Feemster.—p. 54.
Influence of Position on Breath Sounds. A. Kerr Jr.—p. 58.
Radiology in Bone Pathology. J. Hanelin and L. L. Robbins.—p. 60.

Detection of Diabetes.—Diabetes case-finding has been carried on since June, 1947, as part of a community diabetes control program in Brookline, Mass. The case-finding procedure comprised three phases: screening, reexamination, and diagnosis. Of 3,186 persons on whom both blood and urine sugar tests were made, 338 (10.6%) had blood sugar readings above the minimum screening levels and 451 (14.1%) had positive urinalyses. It was possible to diagnose diabetes in 71 of the 3,186 persons. If only those subjects with more than a trace of glycosuria (4% of the total group) had been reexamined, only 40 of the 71 cases would have been found. If only those subjects with blood sugar readings above the levels that screened out 4% of the group had been reexamined, 58 of the 71 cases would have been discovered. By reexamining approximately the same number of persons (4% of the total group) on the basis of the urine sugar screening test and the blood sugar screening test, the specificity of the two tests was compared. Of those singled out for reexamination by the urine sugar test, 35.7% were "new diabetics." Of those singled out for reexamination on the basis of the blood sugar examination, 49.2% were new diabetics. It appears that the blood sugar screening test was more sensitive than the urine sugar screening test when equal numbers of subjects were brought back for further testing by each procedure. The increased sensitivity of the blood sugar test was apparently due to its greater ability to detect persons with the milder type of laboratory findings.

North Carolina Medical Journal, Winston-Salem

12:253-308 (July) 1951

Allergic Problems Demanding Prompt Treatment. J. W. Thomas.—p. 253.
Rhinologic Management of Allergy of Upper Respiratory Tract. H. P. Schenck.—p. 262.
Superimposed Infections in Respiratory Allergy. J. W. Thomas.—p. 267.
Ocular Symptoms of Migraine. F. B. Walsh.—p. 271.
Intractable Pain in Neck and Upper Extremities with Particular Reference to Protrusion of Cervical Disks. J. G. Love.—p. 274.
Joint Responsibilities of Public Health Workers and Private Practitioners. J. W. R. Norton.—p. 287.
Congestive Heart Failure. M. T. Gilmour and H. H. Hodges.—p. 290.

Northwest Medicine, Seattle

50:481-556 (July) 1951

Fate of the Aged Hospitalized for First Time in a State Hospital for the Mentally Ill. S. Levy and R. H. Southcombe.—p. 501.
Chronic Nontuberculous Psoas Abscess Due to Internal Appendiceal Stump Fistula. H. M. Blegen, J. H. Armstrong and W. J. Doyle.—p. 506.
Critical Analysis of Recent Advances in Gynecology. R. D. Reekie.—p. 508.
Care and Healing of Traumatic Wounds. J. G. Matthews.—p. 512.

Plastic & Reconstructive Surgery, Baltimore

7:463-560 (June) 1951. **Partial Index**

Use of Full Thickness Hand Skin Flaps in Reconstruction of Injured Fingers. J. S. Horn.—p. 463.
Unoperated Bilateral Complete Cleft Lip and Palate in Adult: Case Report and Comments. A. D. Davies.—p. 482.
*Effect of ACTH on Survival of Homografts in Man. H. Baxter, C. Schiller, J. H. Whiteside and others.—p. 492.
Treatment of Malunion Fractures of Facial Bones. R. O. Dingman and R. L. Harding.—p. 505.
Salvaging Seriously Injured Hands and Feet. A. G. Bettman.—p. 520.
Observations on Pharyngeal Flap Operation for Improvement of Speech in Cleft Palate Patients. F. S. Dunn.—p. 530.

ACTH and Survival of Homografts.—Four homografts were applied to three patients. Treatment with corticotropin (ACTH) was delayed for 15 days after the application of one homograft, was started on the same day as skin-grafting in two grafts, and in one patient was carried out for six days before the homograft was applied. In this way the timing of the effect of corticotropin on the homografts was varied, so that possible differences in reaction during the sequence of stages of healing of a graft could be observed. All the homografts eventually sloughed. In only one instance were the major blood groups and Rh factor of the skin graft donors and recipients compatible, and in this instance the homograft sloughed off in the customary fashion. The author stresses the often observed rapidity with which a homograft will slough and the granulating area will be resurfaced with epithelial ingrowth from the margins. The "active immunity" theory, which attempts to explain the incompatibility and eventual loss of skin homografts due to an antigen-antibody response appears to receive no support from these results with corticotropin, which is known to block the symptomatic manifestations of certain allergic and anaphylactic reactions.

FOREIGN

Acta Chirurgica Scandinavica, Stockholm

101:259-338 (May 31) 1951

Effect of Sympathectomy on Femoral Artery in Adductor Canal. S. Annersten.—p. 262.
*Pathologicoanatomical Changes Following Rapid and Slow Thawing, Respectively, in Frozen Skin in Man: Experimental Study. J. Adams-Ray and B. Falconer.—p. 269.
Administration of Heparin. J. E. Jorpes, H. Boström and A. E. Roch-Norlund.—p. 279.
Surgical Treatment of High-Situated Gastric Ulcers. Å. Grevillius. —p. 285.
Cause and Incidence of Delayed Nephrectomy After Resections of Kidney. L. Thorén.—p. 291.
Incarcerated Inguinal Hernia in Childhood. O. Wiklander.—p. 303.
Luxation of Distal Radio-Ulnar Joint. A. Birch-Jensen.—p. 312.
Fibrous Dysplasia of Bone. L. Önne.—p. 318.

Changes Following Rapid and Slow Thawing in Frozen Skin.—Before World War II it was generally accepted that the best method of treatment of the ischemic stage of frostbite was slow thawing with snow or ice water; rapid warming was said to cause gangrene. Then opinion changed and treatment with warmth not exceeding the body temperature was advised. Adams-Ray and Falconer carried out experiments on the lower extremities of patients about to undergo amputation because of obliterating processes of the arteries (in one case, for sarcoma in a girl, 16). Immediately below the site of the planned incision freezing with ethyl chloride was done simultaneously on the medial and on the lateral aspects. The frozen area on one side of the legs was rapidly warmed with moist compresses 37 C. The other side was allowed to thaw slowly under the bedclothes. During the amputation, which was performed 24 hours later, the outlined areas of skin were excised and examined. Three of the 21 cases showed no difference between the rapidly warmed and the slowly thawed areas, 3 cases showed more extensive changes after rapid warming, while 15 cases showed greater changes, mainly degenerative, after slow thawing.

Acta Oto-Laryngologica, Stockholm

39:95-272 (May) 1951. **Partial Index**

Studies on Psychology of Hearing. A. V. Christensen.—p. 95.
Clinical, Bacteriologic and Pathoanatomic Considerations in Chronic Tonsillitis. K. Christoffersen and N. G. Richtnér.—p. 102.
*Changes in Inner Ear Following Treatment with Streptomycin. K. Graf. —p. 121.
Comparative Investigations of Different Auditory Fatigue Tests. L. Greisen. —p. 132.
Case of Lingual Herpes Zoster with Homolateral Facial Paralysis. O. Jepsen.—p. 172.
*Erythroblastosis Fetalis and Deafness. S. Johnsen.—p. 176.
Bilateral Failure of Acoustic Nerve Following Unilateral Fenestration. P. Menck-Thygesen.—p. 210.
Effect on Acute Otitis Media of Dipenicillin Administered Once Daily, with Particular Reference to Bacteriology. J. C. Nielsen.—p. 222.

Changes in Inner Ear Following Treatment with Streptomycin.—Graf made histological studies of the petrous part of the temporal bones of 24 patients who had received intramuscular and intrathecal injections of streptomycin for the treatment of tuberculous meningitis. It had been suggested that the auditory disturbances in such patients could be due to the disease as well as to the treatment with streptomycin. In some of these patients, the hearing and vestibular apparatus had been tested while they were undergoing treatment. There was a discrepancy between the impairment in the vestibular and cochlear functions on the one hand and the morphologically demonstrable tuberculous changes in the ear. Histological studies on the terminal acoustic apparatus could be made in 11 of the 24 patients, including three of the six who had become deaf. In all three of these deaf patients the hair cells of the organ of Corti were damaged in the lower and median portions and there was also atrophy of the striae vasculares in this region. Corresponding histological changes were present in some cases also in the sensory cells of the maculae and cristae in the vestibular apparatus. These degenerative changes in the terminal sensory cells correspond to the changes observed in the ears of experimental animals following administration of streptomycin. The author concludes that in the human subjects these changes were the result of streptomycin therapy rather than of the tuberculous meningitis.

Erythroblastosis Fetalis and Deafness.—A girl, born two or three weeks before term, had icterus neonatorum, anemia gravis, and erythroblastosis fetalis at birth. The jaundice lasted more than five weeks. Later, when the importance of the Rh factor in erythroblastosis fetalis was realized, the child and the mother were examined and it was found that the mother was Rh negative and the child Rh positive and that the mother's blood contained Rh antibodies for the red blood cells of the child. The mother had noticed reduced hearing in the child when the latter was about 3 years old. The child began to speak late and had repeated attacks of otitis media, for which paracentesis had been done. She has been obliged to attend a school for the hard-of-hearing. At the age of 11, her hearing is severely impaired in both ears. Although several reports on deafness resulting from erythroblastosis fetalis have appeared in the American and particularly the British literature, this is the first case reported in the Scandinavian countries.

Archiv für klinische Chirurgie, Heidelberg

268:341-446 (No. 4) 1951. **Partial Index**

General Pathological Considerations on Narrowing of Intervertebral Foramens. P. Duus, G. Kahlau and W. Krücke.—p. 341.
Bronchospasm as Complication of Anesthesia. R. Frey, O. Just and E. v. Lüttichau.—p. 363.
Significance of Bronchospirometry in Surgery of the Lungs. J. Maurath. —p. 375.
*Relationship Between Adrenal Cortex, Operative Risk and Postoperative Course, Demonstrated by Changes of Differential Blood Picture and of Eosinophils. J. Rehn.—p. 417.

Relationship Between Adrenal Cortex, Operative Risk, and Postoperative Course.—In patients who had been operated on for various diseases and in whom the course of the disease was normal the author found a typical decrease in lymphocytes about six hours after the operation, followed by a slow increase. Leucocytes showed the reverse behavior, i. e., a pronounced increase followed by a slow decrease. The eosinophils were postoperatively decreased and then slowly increased to above the initial level. An atypical postoperative differential picture with a postoperative increase in lymphocytes and simultaneous decrease in granulocytes was observed in a patient, 55, in whom a neurinoma with cystic degeneration was revealed by operation in the area of the pancreas. Circulatory failure resulted in death on the second postoperative day. The postoperative lymphocytosis suggested failure of the adrenal cortex as the cause of death. Graphic curves of changes in the number of circulating eosinophils in 32 patients operated on for various diseases with an uneventful postoperative course showed a maximum decrease on the first and second postoperative day followed by an increase surpassing the initial level up to the seventh postoperative day. Unlike Coppinger and Goldner, the author did not observe a more pronounced and protracted drop in eosinophils in patients who were subjected to serious operations of long duration. A minor intervention in a patient who is a poor operative risk may induce a greater and longer lasting drop in eosinophils than a major operation in a patient with good resistance to the operative trauma. Results of this study agree with those of Coppinger and Goldner in that the older patients showed a more pronounced depression in the number of circulating eosinophils and a delayed recovery, i. e., a delayed restoration to normal of adrenal cortical activity. Changes in the number of circulating eosinophils were observed in all patients with postoperative complications. A reduction following an increase in eosinophils demonstrates that a new stress had been put on the adrenal cortex. Febrile postoperative bronchitis delayed the increase in circulating eosinophils, while postoperative pulmonary infarction caused a renewed drop. Eosinophil counts were performed before the operation and postoperatively on seven patients who died within 2 to 11 days after the operation. Some of these had very low initial eosinophil values before the operation, indicating the great operative risk. The very low postoperative eosinophil count suggested an additional load placed on the adrenal cortex by the operative trauma. The corticotropin (ACTH) test is a valuable aid in ascertaining prior to surgical intervention the response of the adrenal cortex to a stress similar to operative trauma.

V 14
1951

Archivio di Tisiologia (Scientific Section), Naples

6:299-430 (April) 1951

Roentgenographic Examination in Intracavitary Suction Drainage. G. Torelli.—p. 299.
Intracavitary Suction Drainage Combined with Thoracoplasty in Treatment of Pulmonary Tuberculosis. D. Parmeggiani.—p. 339.
Anatomic Aspects and Results of Process of Healing in Tuberculous Cavities of the Lung Treated with Intracavitary Suction Drainage. A. Blasi.—p. 369.
*Late Results of Intracavitary Suction Drainage with 170 Roentgenographs. P. Marconi.—p. 405.

Late Results of Intracavitary Suction Drainage.—Results are reported of clinical and roentgenologic follow-up examination on 85 patients with various types of cavitary pulmonary tuberculosis, 2 to 12 years after intracavitary suction drainage according to Monaldi's technique. This treatment was employed during the period 1938 to 1942, when antibiotic therapy had not yet been introduced and the technique of obliteration of the draining bronchi had not been developed. The size of the cavities varied from small to giant. Intracavitary suction drainage had been preceded in a few patients by artificial pneumothorax and anterolateral thoracoplasty. In others it was combined with thoracoplasty. In the majority intracavitary suction drainage was the only type of treatment. All of the patients were cured; they were able to resume their work as farmers, lumbermen, factory workers, and soldiers, and are today leading a normal life. Some of the women have married and have had normal pregnancies. Complete and permanent recovery of these patients proved that Monaldi's method of intracavitary suction drainage deserves a definite place in the treatment of pulmonary tuberculosis.

Beiträge zur Klinik der Tuberkulose, Heidelberg

105:189-300 (No. 3) 1951. **Partial Index**

Bronchial Spasm and Adrenalin Test. A. Bühlmann and T. Wegmann.—p. 189.
Pathologic-Anatomic Aspects of Tuberculous Leptomeningitis with Special Consideration of Vascular Processes. A. Witte.—p. 199.
Renal Tuberculosis and Relation to Bone Tuberculosis. H. Berg.—p. 240.
*Purpose and Prospects of Fusion with Bone Splints in Tuberculosis of Bones and Joints. W. Legal.—p. 243.
Plasma Proteins and Tuberculosis. K. Jahnke and W. Scholtan.—p. 249.
Treatment of Fistulizing Tuberculosis of Bones and Joints. W. E. Reinhard.—p. 282.

Fusion with Bone Splints in Tuberculosis of Bones and Joints.—Perhaps the greatest difficulty in the conservative treatment of tuberculosis of the bones and joints is that it is lengthy. The immobilization and protection provided by plaster casts, plaster beds, and bed rest in the horizontal position must generally be continued for years, if the tuberculous lesion in bone or joint is to be healed. In surgical fusion by means of bone splints, however, the period required for complete rest and fixation in plaster can be shortened, for, once the implanted bone splint has healed in place and consolidated, the immobilization obtained is definitely superior to results obtained with plaster casts. Fusion by bone splints also reduces the danger of relapse of the tuberculous process. The time of wearing orthopedic supports can be reduced, and the supports can sometimes be simplified. Ankylosis by means of a bone splint permits painless function and load-bearing for the diseased member. Secondary contractures and other defects can be avoided by bone fusion.

Biochemical Journal, London

49:129-256 (July) 1951. **Partial Index**

Chemical and Electrical Energy Relations for Stomach. E. E. Crane and R. E. Davies.—p. 169.
Preparation of Soluble Cholinesterases from Mammalian Heart and Brain. M. G. Ord and R. H. S. Thompson.—p. 191.
Apparent Protein in Human Urine: Some Surface Film Measurements. A. L. Tárnoky.—p. 205.
Studies on Analysis of Vitamins D: IV. Studies on Irradiation of Ergosterol and 7-Dehydrocholesterol and Analysis of Products for Calciferol, Vitamin D_3, and Component Sterols. J. Green.—p. 232.
Studies on Analysis of Vitamins D: V. Chemical Determination of Vitamin D in Fish-Liver Oils and Other Materials Containing Vitamin A. J. Green.—p. 243.
Inhibition of Histaminase by Amidines. H. Blaschko, F. N. Fastier and I. Wajda.—p. 250.

British Journal of Experimental Pathology, London

32:51-156 (April) 1951. **Partial Index**

Study on Hyperglycaemic Factor in Urine of Psychotics. J. W. Walker and W. Mayer-Gross.—p. 51.
Reaction of Adrenal Cortex to Adrenaline Stress and Identification of Endogenous Liberated Sugar-Active Corticoid by Histological Bio-Assay Technique. T. Symington.—p. 58.
*Effect of Cortisone on Wound Healing. A. D. Bangham.—p. 77.
Growth of Influenza Viruses and Newcastle Disease Virus in Mouse Brain. H. J. F. Cairns.—p. 110.
Alkaline Phosphatase Levels in Plasma and Liver Following Carbon Tetrachloride Administration. V. R. Talageri, K. D. Samarth, A. J. Baxi and P. R. Venkataraman.—p. 118.

Cortisone and Wound Healing.—Earlier reports have shown that in patients with hyperadrenalism wounds heal poorly. In patients receiving corticotropin (ACTH), open wounds, incised abscesses, and biopsy sites failed to show normal granulation tissue and were slow to heal. Corticotropin depressed the formation of granulation tissue in experimentally produced wounds. The authors studied the effect of cortisone on experimentally produced wounds and fractures in animals. They found that the reparative processes were greatly depressed and concluded that the response represented an "inhibition of reactivity." In the present investigation the effects of cortisone on wound healing in different animals are described, and some observations on the effects of cortisone on intracutaneous histamine and a solution of leucotactic peptides are reported. It was found that cortisone has no effect on wound healing in guinea pigs; it probably reduees the amount of granulation tissue formed by rats, and retards wound healing in rabbits. Solutions of leucotactic peptides and of histamine were injected into the skin of rabbits, and the effect of cortisone on the formation of the wheals was observed. These experiments confirm the results of other workers and show that at a relatively high dose level in rabbits the process of wound healing may be retarded. The demonstration that cortisone may inhibit the skin reactions to histamine and leucotactic peptides suggests a mechanism whereby inflammatory and the subsequent reparative processes are subdued. A hypothesis that cortisone reduces the inflammatory response of the tissues would also explain the known effects of the drug in rheumatic fever and rheumatoid arthritis, both conditions representing an exaggerated inflammatory response.

British Journal of Urology, Edinburgh

23:97-196 (June) 1951. **Partial Index**

Treatment of Prostatic Calculi by Perurethral Operation. R. O. Ward.—p. 97.
Renal Failure Following Ureterocaecostomy. A. Kekwick, J. W. Paulley, E. W. Riches and R. Semple.—p. 112.
Development of Trigone of Bladder. D. I. Williams.—p. 123.
Congenital Recto-Urinary Fistula. R. L. Stewart and J. A. Ross.—p. 129.
Primary Carcinoma of Male Urethra. R. C. Alexander.—p. 139.
Multilocular Cysts of Kidney. T. Powell, R. Shackman and H. D. Johnson.—p. 142.
Urethral Stricture Following Prostatectomy. T. W. Mimpriss and M. T. Pheils.—p. 153.
*Fibrinoma of Bladder. R. Marcus and A. C. Brewer.—p. 156.
Report on Renal Actinomycosis. J. K. Willson-Pepper.—p. 160.

Fibrinoma of Bladder.—Fibrinous, albuminous or blood-clot pseudovesical calculi are uncommon. Two cases of fibrinoma of the urinary bladder are reported. In the first, the fibrinoma occurred a long time after excision of a papilloma of the bladder and was discovered on routine cystoscopic follow-up. In the second, the fibrinoma was discovered during cystoscopy, which was necessitated by intractable cystitis following prostatectomy. The first patient refused surgical intervention and died from ascending pyelonephritis. Fibrinomas of the bladder may grow rapidly and may even fill the viscus. Generally, they are few in number and form in infected urine. They may not be recognized on sounding the bladder as they are soft or putty-like in consistency. The lamellated appearance is characteristic and on section resembles an onion. Radiological diagnosis is possible, as the calcium or phosphate in the calculus renders it radiopaque. Intravenous pyelography is of value when crystalloids are present in sufficient quantities to cast a good shadow. A filling defect due to the fibrinoma may be detected in the cystogram. The final diagnosis rests on the cystoscopic findings. Hemorrhage in the presence of certain organisms seems to be a precipitating factor, which may

explain the sudden onset and rapid increase in size. If such is the case, the term "blood stones" is more accurate. Periodic follow-up after removal of fibrinomas is advisable. They may recur and, if not treated, produce renal failure from ascending pyelonephritis.

British Medical Journal, London

2:76-132 (July 14) 1951

*Surgery of Spleen. J. Learmonth.—p. 67.
Mesencephalitis and Rhombencephalitis. E. R. Bickerstaff and P. C. P. Cloake.—p. 77.
Aortic Aneurysm Associated with Arachnodactyly. M. F. Moses.—p. 81.
Persistent Anxiety and Tachycardia Successfully Treated by Prefrontal Leucotomy. G. D. F. Steele.—p. 84.
Congenital Afibrinogenaemia. C. C. de Silva and R. S. Thanabalasundaram.—p. 86.
Corneo-Scleral Suture in Cataract Extraction. H. B. Stallard.—p. 88.
Multiple Spontaneous "Pseudo-Fractures" of Bone (Milkman's Syndrome). S. Nowell, P. R. C. Evans and F. Kurrein.—p. 91.

Surgery of the Spleen.—Learmonth discusses surgery of the spleen on the basis of his own experiences in 123 operations. There were 16 surgical deaths. The indications for splenectomy were orthodox. The author stresses the following observations: 1. The rapidity with which symptomatic improvement usually occurs after splenectomy for idiopathic thrombopenic purpura and for congenital hemolytic anemia. If one ligates the splenic artery at operation for idiopathic thrombopenic purpura and waits long enough before completing the removal of the spleen, the bleeding time falls, although the spleen is receiving an adequate arterial blood supply. 2. The curious lack of uniformity in size of the diseased spleens. In idiopathic thrombopenic purpura the spleen is rarely much enlarged; yet an accessory spleen produces the disease clinically only after its size has increased. In congenital hemolytic anemia the spleen is enlarged; again an accessory spleen must grow before it produces the disease clinically. Apparently, a critical quantitative factor is involved, in amount of toxic substance, the volume of spleen pulp, or the amount of reticuloendothelial tissue. 3. The temporary disappearance of hypersplenism after ligation of the splenic artery, caused possibly by cessation of most of the blood flow through the spleen or reduction in size of the spleen. In either case, again the quantitative factor is apparent. 4. The rapidity with which death follows splenectomy in acute leukemia, although the operation has been easy and the macroscopic appearance of the tissues at necropsy (including the site of operation) uninformative. 5. The rapidity with which splenectomy will terminate acquired hemolytic anemia in some cases of undetermined etiology. These problems await solution by hematologists. In the meantime the author proposes to continue to use splenectomy as a therapeutic measure when it is not definitely contraindicated.

Canadian Medical Association Journal, Montreal

65:1-94 (July) 1951

*Senile Dementia—New Explanation of Its Causation. M. Fisher.—p. 1.
Preventive Procedures in General Practice. J. M. Mather.—p. 7.
Cardiovascular Effects of Triethanolamine Trinitrate—Experimental Study. K. I. Melville and F. C. Lu.—p. 11.
Triethanolamine Trinitrate (Metamine) in Treatment of Angina Pectoris: Preliminary Report. J. H. Palmer and C. G. Ramsey.—p. 17.
NPH Insulin. M. Jamieson, A. H. Lacey and A. M. Fisher.—p. 20.
NPH Insulin: Preliminary Report. K. A. Swallow and A. L. Chute.—p. 23.
*Effect of Cortisone on Nephrotic Syndrome Occurring in Diabetics. C. B. Holmes, G. C. Walsh, M. M. Baird and others.—p. 26.
Transurethral Prostatic Resection—1,000 Cases. C. B. Stewart and J. R. Taylor.—p. 29.
*Intravenous Use of ACTH. H. W. McIntosh and C. B. Holmes.—p. 33.
Palliative Gastrostomy for Inoperable Carcinoma of Oesophagus. J. C. Dickison.—p. 35.
Management of Surgical Shock in the Poor Risk Patient. W. G. Bigelow, J. F. R. Fleming and A. G. Gornall.—p. 37.
Concept and Management of Low Backache. W. B. Parsons.—p. 43.

Cause of Senile Dementia.—Mental deterioration following strokes, due to hemorrhage, thrombosis, or embolism, is usually classified as arteriosclerotic. Yet there is still a large number of cases in which deterioration has been slowly progressive and unmarked by a definite cerebrovascular accident. In this group, diagnosis is most difficult. If the dementia appears around the age of 50, Alzheimer's or Pick's disease is diagnosed. At a later age the diagnosis rests between cerebral arteriosclerosis and so-called senile dementia, but it is problematical if any definite difference exists between these two. When vessel changes are minimal, senile dementia is diagnosed. When they are severe, arteriosclerotic dementia is favored. A pathological study of a case of severe senile dementia uncovered a previously unsuspected lesion. At postmortem virtually complete occlusion of the cervical portion of both internal carotid arteries was found, the intracranial cerebral vessels themselves being almost free of arteriosclerosis. Some 10 other cases of mild and severe dementia have since been studied clinically, and carotid disease, unilateral or bilateral, is suspected in each case. Blockage of one or both carotid channels would explain many pathological features of carotid disease. This causal theory has important therapeutic implications, for the disease would be open to surgical attack. Anastomosis should be feasible in the cervical portion of the internal carotid artery. Carotid occlusion may provide the basis for a unified concept of some of the variegated mental disturbances of old age. It may help to explain senile muscular rigidity, as in one case reported, and the coarse tremor of old age, as in another case. There is evidence that occlusion of the left internal carotid artery, the main supply of the dominant hemisphere, is especially related to the development of dementia.

Cortisone in Nephrotic Syndrome in Diabetes.—The authors used cortisone in three patients with the nephrotic syndrome in diabetes of long standing. All three required more than 30 units of insulin a day. Cortisone was given in 50 mg. doses twice daily by intramuscular injection for 36 or 37 days. Initially, all three patients showed decreased carbohydrate tolerance, as evidenced by raised blood sugar or increased requirement for insulin. In one patient, there was a decrease in insulin requirement after three weeks. Possible reasons for this are discussed. Increased proteinuria occurred in all patients. There was no change in the nephrotic state in two of the patients. In the third, in whom temporary improvement occurred, postmortem examination suggested that the patient had chronic nephritis.

Intravenously Administered Corticotropin.—McIntosh and Holmes attempted to determine the most effective intravenous dosage schedule for corticotropin. In the first patient dosage was increased over a constant period of 24 hours. In the second, a constant dosage of 20 mg. was used, but it was administered over varying lengths of time. The following conclusions were reached: 1. The degree of adrenocortical stimulation attained by continuous intravenous administration of corticotropin is significantly greater than that achieved by the intramuscular route. 2. Maximum stimulation occurs with the relatively small intravenous dose of 10 mg. given continuously over 24 hours. 3. The degree of stimulation measured over a 24 hour period is proportional to the length of time over which the corticotropin is given, being maximal when corticotropin is administered over the whole 24 hour period. 4. The continuous intravenous administration of corticotropin is the most efficient and economical method of achieving adrenocortical stimulation.

Deutsche Zeitschrift für Nervenheilkunde, Heidelberg

165:531-644 (No. 6) 1951

Pathogenesis of Reactions After Encephalography. B. Borschel.—p. 531.
Diphtheria and Diphtherial Nerve Lesions. H. Tellenbach.—p. 557.
*Clinical Epidemiologic Studies on 1947 Epidemic of Poliomyelitis in Hamburg: Significance of Predispositional and Exogenic Factors for the Clinical Course. R. C. Behrend and K. Hansen.—p. 597.
Histological Studies on Plexus Myentericus of Stomach. R. Greving.—p. 622.

Epidemic of Poliomyelitis.—During the 1947 epidemic of poliomyelitis in Hamburg a total of 446 cases were studied. Poliomyelitis was especially frequent in the age groups 6 to 15 years and 16 to 30 years. With increasing age the number of females with the disease increased; however, at all ages the disease was commonest in males. The monophasic and biphasic forms as well as the meningitic and cerebrospinal forms appeared with about the same frequency in all age groups. Purely spinal pictures were more frequent in patients over 30 than in younger persons. Of 259 patients with the cerebrospinal form of polio-

V 14
1951

myelitis four-fifths had the purely spinal form; the rest were about equally divided between bulbar-mesencephalic and mixed spinobulbar and mesencephalic forms. The purely encephalitic form was found in only four of the patients. In 43 patients Landry's paralysis developed and terminated in death. Of the 259 patients who had paralytic symptoms 51 died. In 47 the paralytic symptoms had completely disappeared at the time of discharge from the hospital. In 87, mild disturbances remained; 56 were not able to work because of residual symptoms; and 18 were so severely crippled that presumably they would always have to depend on aid from others. Residual symptoms were more frequent in adults than in children. The age of the patient was found to be more important than the type of virus in determining the form of the disease. Indisposition or physical exertion preceded the onset in 27% of the patients, and it was found that these factors are more important in the higher age groups than in children, that they lead oftener to the cerebrospinal than to the meningitic form of poliomyelitis and seem to produce a higher mortality rate. Nine of the 183 female patients were pregnant. Pregnancy did not seem to predispose to a certain form of the disease. There was nothing unusual in the course of the poliomyelitis in the five patients who had received immunizing injections shortly before the onset.

Edinburgh Medical Journal

58:261-308 (June) 1951

Indications for Surgery in Peptic Ulcer. N. C. Tanner.—p. 261.
Operative Methods in Treatment of Peptic Ulcer. N. C. Tanner.—p. 279.
Oesophageal Ulcer and Treatment of Complications of Peptic Ulcer. N. C. Tanner.—p. 293.

58:309-348 (July) 1951

Vitamin B_{12} and Folic Acid in Megaloblastic Anaemias. R. H. Girdwood.—p. 309.
Occupational Therapy in Mental Hospital: Problem of the Continued Treatment Patient. J. M. Macdonald and H. M. Lewis.—p. 336.

Irish Journal of Medical Science, Dublin

306:241-296 (June) 1951

Parathyroid Carcinoma. D. K. O'Donovan, H. S. Meade and J. McGrath.—p. 241.
*Primary Site of Action of Parathyroid Hormone. D. K. O'Donovan.—p. 252.
Some Recent Developments in Industrial Medicine. L. G. Norman.—p. 265.
Functions of Medical Service in Industry. B. Pringle.—p. 269.
Prevention and Control of Disease in Industry. J. F. Eustace.—p. 274.
Accident Prevention and Rehabilitation. I. R. Moore.—p. 279.
Haemorrhage from Coronary Vessels of Uterine Myoma. V. Sheehan.—p. 285.
Apparatus for Resuscitation of Newborn. P. K. Storah.—p. 289.
Unusual Case of Duodenum Inversum. S. O'Beirn.—p. 293.

Site of Action of Parathyroid Hormone.—O'Donovan mentions three theories of the primary site of action of parathyroid hormones, pointing out that there is little difference between Albright's (1929) and Helfit's (1940) theories, since both stress the importance of urinary phosphate excretion. O'Donovan cites clinical observations that conflict with this theory: 1. The symptoms of rapidly growing tumors of the parathyroid indicate that bone lesions will always occur in hyperparathyroidism if the tumor secretion is sufficient. 2. Retention of inorganic phosphate in the blood has no inhibitory effect on either the symptoms or the biochemistry of severe hyperparathyroidism. 3. The biochemical changes that immediately follow removal of a parathyroid tumor indicate that the hormone acts directly on bone, since the serum inorganic phosphate level remains low and calcium phosphate is rapidly deposited in the bones. 4. The facts recorded in the literature concerning Fanconi's syndrome are incompatible with the renal phosphate theory. 5. It is difficult to reconcile the occurrence of metastatic calcification in hyperparathyroidism and in 14 cases of postoperative tetany with the renal phosphate theory. 6. Observation of the changes in serum calcium and phosphate in tetany do not indicate that changes in phosphate control the changes in calcium. The hypocalcemia and hyperphosphatemia have an approximately linear relationship, and the former precedes the latter.

Journal of Mental Science, London

97:441-634 (July) 1951. **Partial Index**

Inheritance of Neuroticism: Experimental Study. H. J. Eysenck and D. B. Prell.—p. 441.
Intelligence and Modern Social Trends. E. O. Lewis.—p. 468.
Surgical Uncertainties of Prefrontal Topectomy and Leucotomy (Observations on 100 Cases). J. Le Beau.—p. 480.
Phenylpyruvic Oligophrenia. V. Cowie.—p. 505.
Psychoses in Childhood. M. Creak.—p. 545.
Evaluation of Electric Convulsion Therapy as Compared with Conservative Methods of Treatment in Depressive States. E. T. O. Slater.—p. 567.
Sub-Acute Sclerosing Leuco-Encephalitis: Clinical and Pathological Report of Two Cases. J. A. N. Corsellis.—p. 570.
*Alien's Paranoid Reaction. F. F. Kino.—p. 589.

Alien's Paranoid Reaction.—The authors report a peculiar paranoid reaction in a group of young men of Polish nationality who were admitted to a mental hospital in Britain. They had arrived in Britain after the war, and as long as they continued to live within their own units or groups they felt contented. The change occurred with their transfer to workshops or pits, where they found themselves isolated in a foreign environment where the language and habits were unknown to them. Misunderstandings unavoidable in such a situation evoked their suspicion and mistrust. Gradually, this morbid state of mind grew to such intensity that a rational appreciation of the environment became impossible. The progressive emotional tension culminated in several instances in a state of elemental panic and confusion, with impulsive running away or suicidal preoccupations. Some of them had vivid visual or auditory hallucinations whose content was closely connected with their delusional preoccupations. With nonspecific psychotherapy, supported by electroshock therapy, and, in one case, by insulin shock treatment, they became gradually more adjusted, with more and more insight into the abnormality of their feelings and ideas, and were eventually able to return to their former surroundings and occupations.

Lancet, London

2:45-86 (July 14) 1951

Traumatic Intracranial Haematoma. T. G. I. James and E. A. Turner.—p. 45.
Organisation of Syringe Service. J. F. Horley.—p. 50.
Hospital Syringe Service. A. Gibson.—p. 52.
*Hormonal Treatment of Simmonds's Disease. J. D. Robertson and H. F. W. Kirkpatrick.—p. 54.
Laburnum Poisoning in Children: Report of 10 Cases. R. G. Mitchell.—p. 57.
Prognosis of Healed Gastric Ulcers. B. Barsby.—p. 59.
Atresia of Ascending Colon. J. Jemson.—p. 61.
Activity of Anti-Histamine Drugs: Method of Assessment in Man. A. A. C. Ross.—p. 62.
Mastoiditis Treated with Penicillin and Other Antibiotics. W. McKenzie.—p. 63.

Treatment of Simmonds' Disease.—A man, 47, acquired Simmonds' disease from traumatic hemorrhage into the pituitary. He had been given implants of desoxycorticosterone, 400 mg., and of testosterone propionate, 400 mg., in September, 1947, and was taking 60 or 120 mg. of thyroid and a liberal amount of salt daily. Later, he discontinued this treatment, and in August 1950 his condition had so greatly deteriorated that he was hospitalized. He was then treated with injections of corticotropin (ACTH). On the fifth day a sense of well-being developed, which lasted up to two weeks after completion of the course. The most efficacious dosage seemed to be 60 mg. daily. When treatment with cortisone was begun, 30 days after the corticotropin course, the patient had again lost most of his vigor. With injections of cortisone the patient had severe bouts of depression. Two weeks after he had received implants of desoxycorticosterone acetate and testosterone propionate, as well as thyroid by mouth, he regained his sense of well-being. Cortisone seemed less effective than either of the other treatments. No ill effects followed 32 days of corticotropin therapy, with a total dose of 2.3 gm., nor 22 days of cortisone therapy, with a total dose of 2.2 gm. The investigations lasted four months. The treatment led to a gain of 23½ lb. (10.6 kg.) in weight, a rise in blood pressure from 100/65 to 145/90 mm. Hg, a rise in basal metabolic rate from —40% to —13%, and much general improvement in health. No improvement took place in the im-

paired carbohydrate metabolism, and this awaits further study. Experimental work suggests that absence of the growth hormone may play a part in the causation of the hypoglycemia. Other reports on the use of corticotropin and cortisone in Simmonds' disease are reviewed.

2:87-130 (July 21) 1951

Leucotomy in Psychosomatic Disorders. W. Sargant.—p. 87.
Rostral Leucotomy. W. McKissock.—p. 91.
Effect of Salicylates on Pituitary and Suprarenal Glands. B. S. Hetzel and D. C. Hine.—p. 94.
Direct Method of Measuring Circulating Blood Volume. S. R. Mukherjee and S. Rowlands.—p. 98.
*Nephrotic Oedema Treated with Ion-Exchange Resin. W. W. Payne and R. H. Wilkinson.—p. 101.

Ion Exchange Resin in Nephrotic Edema.—The exchange resins are insoluble nontoxic synthetic resins that can exchange ions present in the resin for other ions in a surrounding solution. Base exchange resins have been used to remove sodium from ingested food, thus simulating the low salt diets used to reduce body fluids in hepatic ascites and cardiac failure. In the present study six children with nephrotic edema were treated with an exchange resin that was unstable above 40 C. and so was incorporated into food when cold. Each gram of resin could absorb cations and liberate hydrion to the theoretical extent of 2.5 mEq. The six children received a high-protein low-salt diet containing about 8 mEq. of sodium ion and 30 mEq. of potassium ion a day. The children ranged in weight from 30 to 50 lb. (13.6 to 22.7 kg.). It was considered that 12 gm. of resin (30 mEq.), increased if necessary to 20 gm. (50 mEq.), would absorb sufficient sodium ion and not produce dangerous acidosis. The children's weight decreased one to four days after the start of resin therapy, and continued to decrease during treatment, sometimes to the expected weight for the age. Within 48 hours of the end of therapy the weight began to increase abruptly and then fluctuated about a mean that was lower than before treatment. Urinary output increased. On two occasions ascites was pronounced, and the resin had no apparent effect on this. During resin therapy the serum potassium levels were depressed but not sufficiently to influence the electrocardiograms. The plasma bicarbonate level fell, and the blood urea level began to rise concurrently. This was regarded as an indication for stopping resin therapy. Low serum potassium levels and metabolic acidosis were treated with potassium citrate, and low serum potassium levels without metabolic acidosis were treated with potassium chloride. Resin treatment appears to be an effective method of reducing edema, but, like all other methods, it is not always successful. In particular it was not effective in reducing ascites. It is necessary to consider the dangers of acidosis, a low serum potassium level, and a raised blood urea level.

Medical Journal of Australia, Sydney

1:745-780 (May 26) 1951

Small Outbreak of Acute Benign Lymphocytic Choriomeningitis. J. Parry.—p. 745.
Syphilis of Pulmonary Artery. C. Engel.—p. 749.
Tigloidine as Substitute for Atropine in Treatment of Parkinsonism. E. M. Trautner and C. H. Noack.—p. 751.
Use of "Perspex" for Splints. J. M. Davies.—p. 754.
Intracranial Abscess Following Frontal Sinus Infection. R. S. Hooper.—p. 756.
*Oligophrenia Phenylpyruvica, or Følling's Disease. S. J. Cantor.—p. 761.
Some Psycho-Physical Aspects of Backache. E. H. Frazer.—p. 763.

Oligophrenia Phenylpyruvica.—In phenylpyruvic oligophrenia, described in 1934 by Følling of Oslo, mental deficiency is associated with the excretion of phenylpyruvic acid in the urine. The acid is easily detected by the addition of liquor ferri perchloridi to the urine. The excretion of this acid is the result of faulty metabolism of the product of the digestion of protein, the amino acid phenylalanine. Phenylpyruvic oligophrenia is hereditary and is transmitted by a single gene. A survey of 1,520 mentally defective patients in Norway revealed 23 patients with phenylpyruvic oligophrenia, and also disclosed that a high degree of consanguinity, such as the marriage of first cousins—if they carried the causative recessive gene—resulted in a higher familial incidence of the malady. The gene influences the nervous system through the phenylalanine-derived toxin, and mental deficiency results. Tremor, muscular rigidity, active deep reflexes, and athetosis may sometimes be noted. Cantor's aim was to call attention to this disorder. He will describe in a later report the three cases of phenylpyruvic oligophrenia that have been found in Victoria. He suggests that other mentally defective patients should be surveyed for excretion of phenylpyruvic acid.

Minerva Ginecologica, Turin

3:245-304 (May supplement) 1951. **Partial Index**

New American Morphological Classification of Female Pelvis Based on Roentgenographic Examination. V. S. Pesce and N. Damiani.—p. 253.
Observations on Vaginal Cytology in Some Mental Diseases. G. Sani and P. Maroncelli.—p. 265.
*Local Therapy of Vulvovaginocervicitis with Sulfonamide Compounds Combined with Penicillin. R. Livio.—p. 290.

Sulfonamides and Penicillin in Vulvovaginocervicitis.—Sixty-nine women, 21 with vulvovaginitis, 33 with vaginocervicitis and 15 with cervicitis, were treated with local application of a sulfonamide compound combined with penicillin. One suppository consisting of 2,000 Oxford units of the sodium salt of penicillin F, G, and X, and of 1 gm. of a sulfonamide compound was applied every evening to the lesions. The next morning the vagina was irrigated with lukewarm water, which had been boiled. Two suppositories were applied daily in a few instances in which one was insufficient. Previous treatment with other compounds had failed in 26 of these patients. Response to this therapy was gratifying. Of the 69 women, 50 were completely cured, and 19 showed pronounced improvement. Twelve patients were cured after six applications, 27 after 12, and in no case were more than 18 applications required. This was the only type of therapy employed. The good results are due to the synergistic action of the sulfonamide compound and penicillin. The course of the treatment was relatively short. The author believes that it could be shortened even more if systematic daily application of the suppositories were combined with medicated irrigation of the vagina and if the amount of penicillin in the suppository were increased to 10,000 Oxford units.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:1789-1856 (June 23) 1951. **Partial Index**

*New Light on Pathogenesis and Therapy of Ménière's Disease. G. A. Hoogland.—p. 1798.
*Infection with Virus of Measles in Therapy of Nephrotic Syndrome. Kho Lien Keng and F. Kuipers.—p. 1806.
Plasma Transfusions in Hemophilia S. van Creveld and M. M. P. Paulssen.—p. 1818.

Ménière's Disease.—Hoogland reviews the theories on the pathogenesis of Ménière's disease and states that he accepts the labyrinthine hydrops as the pathological substrate and believes that disturbances in the vasomotor elements of the labyrinth play a part. He employed blockage of the cervical sympathetic by infiltration of the stellate ganglion in 27 patients with Ménière's disease. He found that vertigo disappeared in nearly three-fourths of the patients; tinnitus aurium decreased in more than a third, and auditory acuity improved in one-fifth of the patients.

Virus of Measles in Nephrotic Syndrome.—Barness, Moll, and Janeway were first to attempt the treatment of children with nephrotic syndrome by infecting them with the virus of measles. The authors cite the results obtained with measles virus in 31 cases of the nephrotic syndrome reported in the literature. They themselves administered measles virus to two patients with glomerulonephritis and the nephrotic syndrome. The virus was administered by intramuscular injection of citrated blood or plasma from patients who either had the exanthem of measles or had had it a few days before. The nephrotic syndrome completely disappeared in one of the patients after several other treatments, including corticotropin (ACTH), had failed. In the second patient the nephrotic syndrome recurred after a temporary improvement.

V 14
1951

Nordisk Medicin, Stockholm

45:951-990 (June 20) 1951. **Partial Index**

Latent Disturbances in Atrioventricular Conduction. O. Ljung.—p. 960.
Neurocutaneous Syndrome Associated with Oligophrenia. J. Oster.—p. 963.
Late Sequels of Hemophilus Influenzae Meningitis: Analysis of 32 Cases. S. Hestetun.—p. 965.
*Late Results of Gold Treatment of Rheumatoid Arthritis. N. Egelius, N. G. Hävermark and G. Nyström.—p. 968.
Methylscopolamine Nitrate Preoperatively to Prevent Excessive Secretion in Respiratory Tract. O. von Dardel.—p. 971.
Transitional Endometrium. B. Törnqvist.—p. 972.

Late Results of Gold Treatment in Rheumatoid Arthritis.—Egelius and his co-workers examined 210 patients with rheumatoid arthritis from 5 to 15 years after gold treatment. The results indicate that long-term prognosis cannot be evaluated from any initial improvement. The results were significantly more favorable in males (28% free from symptoms, 31% improved, 15% unchanged, and 26% worse) than in females (9% free from symptoms, 30% improved, 17% unchanged, and 44% worse). The outlook is better for younger patients. When gold treatment was started within a year of the onset of symptoms the results were notably better than when treatment was begun later. It seems to be important that the first series of treatment be followed in a short time by a new series or that a maintenance dose be established after the first series. The authors now give a maintenance dose of 50 mg. every second or third week.

Schweizerische medizinische Wochenschrift, Basel

81:633-652 (July 7) 1951. **Partial Index**

*Combined Treatment of Tuberculous Meningitis with Streptomycin, Paraaminosalicylic Acid (PAS) and Chaulmoogra Oil. B. Steinmann.—p. 633.
Diagnostic and Prognostic Significance of Changes of Cerebrospinal Fluid in Tuberculous Meningitis, Particularly of the Sugar and Chloride Values, Under Treatment with Streptomycin and in Some Cases with Paraaminosalicylic Acid. H. Gwalter and W. Pulver.—p. 637.
Significance of Pressure in Hysterosalpingography: New Instrument for Measurements of Pressure. C. Müller.—p. 639.

Combined Treatment of Tuberculous Meningitis.—Three women, aged 28, 21, and 53, respectively, with tuberculous meningitis were given combined treatment with streptomycin, paraaminosalicylic acid, and a proprietary mixture of ethyl esters of the fatty acids of chaulmoogra oil (moogrol®). The patients were followed up for 29, 22, and 17 months, respectively. Treatment of the first patient was started with streptomycin alone in doses of 1.5 to 2 gm. intramuscularly per day for the first two weeks and then with daily doses of 1 mg., and intrathecal injections of 150 to 200 mg. daily first, and 50 mg. later. After one month of streptomycin treatment, 1 cc. of moogrol® was given daily for two months in addition to streptomycin. Meningism and vomiting subsided temporarily, but recurrence of symptoms required combined treatment with streptomycin intramuscularly and with paraaminosalicylic acid by intravenous route. Improvement was slow, but was maintained when treatment with paraaminosalicylic acid was continued orally. Combined treatment of the second patient was instituted from the start with streptomycin intramuscularly and intrathecally and paraaminosalicylic acid given first by drip infusion (20 gm. daily) and subsequently orally. The symptoms of meningitis subsided, but there was a recurrence at the end of the fifth month of treatment. Treatment with streptomycin and paraaminosalicylic acid was discontinued for a short time because of severe vomiting, but was resumed and was combined with administration of moogrol.® Definite recovery resulted, suggesting that moogrol® restored the sensitivity of the bacilli, which had become resistant to streptomycin and paraaminosalicylic acid. The third patient was also given from the start combined treatment with streptomycin and paraaminosalicylic acid and, after three weeks of this treatment, was given in addition 1 cc. of moogrol® daily. Recovery from meningitis resulted within six weeks without recurrence. The rapid and favorable course may be ascribed at least partially to the moogrol.® The three patients have been in good health for at least six months and have had no recurrence, but it is premature to attempt definite evaluation of the cure. The retrobulbar neuritis in the first case was caused by the tuberculous meningitis, while permanent vestibular disturbances in all three patients and additional impairment of the auditory nerve in two was caused by streptomycin. Several functional tests of the vegetative regulation were carried out after the patients' recovery, because of the localization of the tuberculous meningitis close to the hypophysis and the diencephalic vegetative centers. Occasional mild disturbances, such as low basal metabolism, delayed water excretion, and disturbances of circulatory regulation, could be demonstrated. Impaired sugar regulation with a tendency to hypoglycemia was observed in all three patients.

Semaine des Hôpitaux de Paris

27:2207-2264 (July 10-14) 1951. **Partial Index**

Bullous Tuberculosis of Infants. R. Debré, R. Grumbach and L. Pichon.—p. 2207.
*Deformities of Vertebral Column in Patients with Congenital Cardiopathies. E. Donzelot, E. Strohl, M. Durand and others.—p. 2216.

Deformities of Vertebral Column Associated with Congenital Cardiopathies.—Of 623 patients with congenital cardiopathies subjected to roentgenologic examination, 172 had deformities of the vertebral column. The 623 patients were divided into two groups, consisting of 506 patients in whom the congenital cardiopathy was associated with cyanosis and of 117 patients without cyanosis. Of the 506 patients, 155 (30%) had deformities of the vertebral column, while 17 (14.5%) of the 117 patients had such deformities. A detailed study of the two groups showed that the incidence of the deformities of the vertebral column varied considerably with the type of the congenital cardiopathy, since of 22 patients with Roger's disease not a one had a deformity of the vertebral column, while of 14 with coarctation of the aorta, five did. Of 121 patients with tetralogy of Fallot, 87 had dextroposition and 34 had sinistroposition of the aortic arch; 69 (79%) of the 87 and 16 (47.6%) of the 34 had deformities of the vertebral column. The lateral deformities of the vertebral column observed in patients with congenital cardiopathies differed somewhat from those of patients with essential scoliosis. The forces which tend to produce essential scoliosis are manifested by a vertical component that induces compensation curvature and vertebral rotation. On the other hand, there is a horizontal tendency in patients with deformities of the vertebral column associated with congenital cardiopathies, which may explain the lower incidence of compensation curvature and vertebral rotation in these patients. The authors believe that every type of cardiopathy may have specific cardiovascular dynamics that determine the pathogenesis of the deformities, while the part played by anoxia seems to be secondary.

South African Medical Journal, Cape Town

25:385-400 (June 9) 1951

Generalized Developmental Osseous Dystrophies: IV. Gargoylism. W. P. U. Jackson.—p. 385.
Skin Sensitivity to Steroid Hormonal Substances: Discussion of Possible Mechanism of Endocrine Allergy. Results of Testing 140 Male and 19 Female Subjects. J. Pepys.—p. 390.
*Role of Vitamin B_{12} in Polyneuritis, Fatty Degeneration and Pernicious Anaemia. P. Menof.—p. 394.

Vitamin B_{12} in Polyneuritis.—Menof recently called attention to the remarkable curative action of vitamin B_{12} in the polyneuritides associated with chronic alcoholism and diabetes mellitus. He reported a dramatic response in nine of 11 cases. Since that time he has treated 12 similar patients (seven alcoholic, four diabetic, and one diabetic and alcoholic). The response has been uniformly satisfactory. The tenderness and volume of the liver receded almost as rapidly as the neurological disturbances. The author feels that vitamin B_{12} should be used wherever fatty degeneration is encountered. It is also indicated in any condition where demyelination or defective red blood cell structure is believed to be the underlying pathological factor. Reasons are given why pernicious (Addison's) anemia should now be regarded as a disorder of lipoid metabolism rather than as a disease of the blood. Evidence is adduced to show that the action of vitamin B_{12} is to synthesize the various chemical substances that make up certain phosphatides or cerebrosides or both.

Thorax, London

6:103-208 (June) 1951

Effect of Posture on Diaphragmatic Movement and Vital Capacity in Normal Subjects with Note on Spirometry as Aid in Determining Radiological Chest Volumes. O. L. Wade and J. C. Gilson.—p. 103.
Experimental Asbestosis in Rats: Effect of Particle Size and of Added Alumina. J. M. Smith, I. D. P. Wootton and E. J. King.—p. 127.
Observations on Haemodynamics of Pulmonary and Lobar Atelectasis. J. C. Gilroy, V. H. Wilson and P. Marchand.—p. 137.
Intradiaphragmatic Mesothelial Cysts. G. Cruickshank and D. B. Cruickshank.—p. 145.
Possible Case of Oedematous Fibroma with Inflammatory Changes. V. Eskelund.—p. 154.
*Intrapleural Haemorrhage in Artificial Pneumothorax. J. T. Harold.—p. 162.
Agenesis of Lung. P. Wexels.—p. 171.
Fatal Acute Iodism After Bronchography. J. Sumner, A. I. Lichter and E. Nassau.—p. 193.

Intrapleural Hemorrhage in Artificial Pneumothorax.—Records of 37 cases with intrapleural hemorrhage of not less than one pint (473 ml.) developing after induction of artificial pneumothorax or after thoracoscopy are reported. The blood should be emptied early after it has entered the pleural space. The aim is to reduce foreign matter to a quantity that the pleura can absorb, and to reduce pleural exudate and so prevent secondary clotting. The first three days are vital, the risk of secondary clotting being reduced by aspiration during this period. Fragmented primary clot or secondary clotting may make further needle aspirations impossible. Thoracoscopic aspiration was performed in seven of nine patients with clotted hemothorax. If clot remains in the pleural cavity despite simple and thoracoscopic aspiration, thoracotomy and clot removal should be undertaken. This measure was used in only two of the 37 cases, and in both the artificial pneumothorax was lost. Before employing operative measures, the use of liquefying enzymes derived from hemolytic streptococci might be considered. They are streptokinase and streptodornase, the former liquefying fibrin and the latter nucleoprotein. When injected intrapleurally the enzymes cause liquefaction of the clotted hemothorax and a severe pleural effusion. A brief febrile reaction generally accompanies these changes, after which simple aspirations are again possible. If bleeding continues, attempts may be made to identify the bleeding point, but in the light of experience with thoracoscopy and thoracotomy carried out for this purpose, such attempts have little place in the early treatment of hemothorax complicating artificial pneumothorax. Decortication of clotted hemothorax is widely used in traumatic cases, but its use with artificial pneumothorax is not advisable, because preservation of the pneumothorax is desired for treatment of the tuberculous lung and because decortication will involve serious risk in patients with active pulmonary tuberculosis. The results obtained with different methods in these 37 cases suggest that simple aspiration is satisfactory. Deaths are rare, most patients do well, and a useful artificial pneumothorax usually remains.

Transactions Royal Soc. Trop. Med. and Hyg., London

44:611-764 (June) 1951. **Partial Index**

Recent Investigations into Treatment of Schistosomiasis by Miracil D in Egypt. J. Newsome.—p. 611.
Four Years' Experience of Sulphone Treatment of Leprosy. J. Lowe and T. F. Davey.—p. 635.
Biological Basis for Campaign Against Malaria Vectors of Brazil. M. Pinotti.—p. 663.
Strain of Monkey Malaria (Plasmodium Cynomolgi) Made Resistant to Proguanil (Paludrine). F. Hawking and J. P. Thurston.—p. 695.
Morphological Changes in Plasmodium Berghei Following Proguanil, Sulphadiazine and Mepacrine Therapy. J. P. Thurston.—p. 703.
Morphological Changes in Plasmodium Cynomolgi Following Proguanil, Sulphadiazine, and Mepacrine Therapy. J. A. McFadzean.—p. 707.
Studies on Protozoa—Part III.—Visceral Leishmaniasis in Cotton Rat (Sigmodon Hispidus). J. D. Fulton and J. S. F. Niven.—p. 717.
*Sickle-Cell Trait and Sickle-Cell Anaemia. H. Foy, A. Kondi and C. Alexandrides.—p. 729.

Sickle Cell Trait and Sickle Cell Anemia.—Foy and associates reason that if the sickle cell trait is regarded as a heterozygous condition (Ss) and sickle cell anemia as a homozygous state (SS), then sickle cell anemia can arise only as a result of the mating of two heterozygous persons (Ss x Ss), of a heterozygous and a homozygous (Ss x SS) person, or of two homozygous (SS x SS) persons. If this hypothesis is correct, then there should be more homozygous sickle cell anemia in a population with a high percentage of the trait than in a population with a low incidence of sickle cell trait. The prevalence of the sickle cell trait among certain of the Negro tribes of Africa, and the reputed absence of sickle cell anemia, means either that the present accepted genetic hypothesis is not entirely correct or that the anemia is far commoner than has so far been reported. Investigations so far carried out in Kenya show that owing to a high infant and/or intrauterine mortality rate in the homozygous, few survive to the age of puberty. If this work is confirmed, then sickle cell anemia should be found often in newborn babies and/or infants, and should be much rarer in adults. If this is the case, then death of the homozygous individual must be an important cause of infant mortality and may be a factor in the small families common in many African tribes. The authors discuss the case of a Greek girl who had sickle cell anemia, which contradicts the theory that sickle cell disease is evidence of Negro ancestry. Furthermore, only one of the patient's parents, the mother, had the sickle cell trait (Ss).

Ugeskrift for Laeger, Copenhagen

113:697-734 (May 31) 1951. **Partial Index**

*Precancerous Changes in Mucous Membrane of Portio; Examination of 104 Cases Observed for at Least Five Years. O. Petersen.—p. 697.
Outbreak of Food Poisoning Due to B. Cereus. O. Christiansen, S. O. Koch and P. Madelung.—p. 703.
Abacterial Meningitis with High Protein Content in Spinal Fluid. H. Letman.—p. 706.
Effect of Neptusan on Seasickness. V. Dyrberg and H. J. Laurtizen.—p. 710.
Raynaud's Disease Due to Protracted Use of Hypnotics? M. Matthiesen—p. 715.

Precancerous Changes in Mucous Membrane of Cervix.—Petersen states that in 104 cases with precancerous changes in the cervix (classified as leukoplakia simplex, leukoplakia with dedifferentiation, and leukoplakia observed for cancer) followed for five to 12 years, cancer developed in 14 (13.5%). In all groups the average age on the first examination in the Copenhagen radium station was 40.2 years. No cancer developed during the observation period in patients in the first group; cancer was found in six of the 30 patients in the second group after from 25 to 62 months, and in eight of the 24 in the third group after from five to 67 months. Control examinations of the changes in the mucous membrane of the cervix every three or four months, if feasible, are advised, especially in patients under 35. In or after the climacteric more radical interventions (total hysterectomy or radiotherapy) may be considered, but in these cases also the outlook for the patient will not, it is thought, be imperilled by a few months' expectant treatment with histological control. The histological picture of the epithelial changes afforded no indication as to possible later development of cancer.

113:773-810 (June 14) 1951. **Partial Index**

*Treatment of Whooping Cough with Chloramphenicol. L. C. Grandjean and H. C. A. Lassen.—p. 776.
Fracture of Body of Femur in Children. E. Naver.—p. 778.
Intussusception of Small Intestine Established on Roentgen Examination. T. Francis and M. Ottsen.—p. 785.

Chloramphenicol in Whooping Cough.—From the results in 100 proved cases of whooping cough treated with chloramphenicol Grandjean and Lassen conclude that this agent provides for the first time treatment for whooping cough effective in the great majority of cases. The treatment was followed by a sharp decrease in the attacks of coughing and by simultaneous notable improvement in the general condition. Chloramphenicol is regarded as indicated in all cases of whooping cough in infants and in graver cases in older children and adults. Determination of resistance of 45 whooping cough strains to chloramphenicol showed no resistant strain.

V 14
1951

BOOK REVIEWS

Handbook of Nutrition: A Symposium Prepared Under the Auspices of the Council on Foods and Nutrition of the American Medical Association. Second edition. Cloth. $4.50. Pp. 717, with 42 illustrations. Published for American Medical Association by Blakiston Company (Division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1951.

This edition of the Handbook of Nutrition is a symposium by some 30 leading authorities in the field of nutrition. Many of the articles were printed in THE JOURNAL during the preceding two years. The book is divided into four parts.

Part 1 is concerned with individual nutrients. The chapter on carbohydrate metabolism is especially well done. It points out that the catabolic pathways of the carbohydrates, fats, and proteins cross at many points and that within wide limits one nutrient may be substituted for another without significant injury to the metabolizing tissue. Each of the three major classes of nutrients may supply organic fragments that feed into the tricarboxylic acid cycle, a sequence of reactions that apparently serves to supply a large portion of the energy need of many biologic systems. As this fusion of metabolic pathways has been elucidated, the classic lines of demarcation between the metabolisms of fat, protein, and carbohydrate have become progressively more obscure and more meaningless. The picture that is developing is one of reaction sequences, often cyclic, that liberate energy as needed by the organism, and these cycles apparently may be fed at many points and in many ways. Part 2 concerns nutritional needs. The chapter on nutritional needs in illness and disease will be of interest to general practitioners. Part 3 deals with nutritional deficiencies. It contains unusually good chapters on caloric undernutrition and fluid therapy.

The last part of the book, on foods and their nutritional qualities, has an interesting and timely chapter on foods for emergencies. It points out that for populations in the path and in the wake of war, finding food becomes a matter of supreme importance. By utilizing edibles disregarded in normal times, much can be done to alleviate or postpone the worst effects of famine. Substantial contributions to the family larder can be made by gardening. By these means sufficient vitamins and minerals are usually obtainable. The pressing problems, then, relate to calories and biologically superior protein.

The Handbook has a reasonably good index. It is a useful addition to the literature of nutrition, a subject that is becoming increasingly recognized as of importance in medicine, both preventive and therapeutic.

Genetics in Ophthalmology. By Arnold Sorsby, Research Professor in Ophthalmology, Royal College of Surgeons, London. Cloth. $9.50. Pp. 265, with 233 illustrations. Butterworth & Co., Ltd., 4-6 Bell Yard, Temple Bar, London, W.C.2; C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

Arnold Sorsby is the author of numerous reports on a variety of ophthalmic subjects, all of great merit. He is also the editor of the important two volumes of "Recent Progress in Ophthalmology." His present contribution is his most important so far.

The subject of genetics is one in which few physicians have more than a passing interest, and very few ophthalmologists have sufficient background to properly interpret the frequent congenital and familial aberrations of the eyes encountered in their daily work. Sorsby is completely aware of this lack of knowledge and wisely, in a simple yet effective way, covers the facts and accepted theories of genetics in the first section of his book. The remainder of his work consists of a discussion of the ocular conditions known or suspected to be of genetic origin. Section 2 describes isolated anomalies occurring in every part of the eyeball and adnexa. Section 3 deals with the relation to ocular lesions of generalized disorders, e. g., metabolic and systemic disturbances, and with syndromes of ocular lesions.

Geneticists have long been aware of the important part that the eye has played in their science and have, along with many ophthalmogists, collected over the years, carefully and painstakingly, pedigrees of their patients. Sorsby has rendered a great service by gathering up these pedigrees from widespread sources and putting them into this relatively small and neat volume. In his preface he points out that the spotlight of medicine has shifted from infections, now for the most part under control, to the constitutional, environmental, and hereditary aspects of disease. "In some affections," he says, "the genetic factor is obvious. In others, it can be revealed only by exhaustive investigations aided by an understanding of genetic theory. The genetic anomalies have assumed greater significance with the recognition of modes of inheritance other than the simple autosomal recessives and dominants of the past. Isolated cases of genetic disease are no longer clinical puzzles and unusual modes of inheritance are more readily recognized."

The illustrations and charts are excellent, the book is beautifully printed, and the indexes are adequate.

Clinical Unipolar Electrocardiography. By Bernard S. Lipman, A.B., M.D., Assistant in Medicine, Emory University School of Medicine, Atlanta, Georgia, and Edward Massie, A.B., M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Missouri. Cloth. $5. Pp. 232, with 191 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1951.

This manual was developed from notes the authors used in teaching unipolar electrocardiography to the students of Washington University School of Medicine. Thus the material contained in this book has stood the test of the classroom. It is intended primarily for those who have had no experience in the subject, so that the presentation is elementary, concise, and at times dogmatic. Almost 200 diagrams and illustrations help to make clear a subject that is ordinarily complicated and difficult to understand.

Unipolar electrocardiography was introduced in 1933 by Frank N. Wilson and his associates. By connecting each of the three arm leads through a 5,000 ohm resistor to a central terminal, an indifferent electrode, which for all practical purposes has a potential of zero, was produced. Thus, the other electrode, known as the exploring electrode, can be placed anywhere on the body to record the electrical potential at that point. At first this technique was used as an important experimental tool, but now it has been shown to be of considerable clinical importance as well. For instance, unipolar electrocardiograms make it possible to determine fairly accurately the electrical position of the heart. The type of bundle branch block, the location of a myocardial infarct, and other electrocardiographic abnormalities are more clearly defined with this method than with the old bipolar, three-lead electrocardiogram.

This is not a textbook on electrocardiography, and such subjects as cardiac arrhythmias and vector electrocardiography will not be found in this book. The authors have limited themselves exclusively to unipolar electrocardiography. For those who are already familiar to some extent with clinical bipolar electrocardiography, this book will form an excellent introduction to unipolar electrocardiography.

The Measurement of Linkage in Heredity. By K. Mather, D.Sc., F.R.S., Professor of Genetics, University of Birmingham. Second edition. Cloth. $1.75. Pp. 149. Methuen & Co., Ltd., 36 Essex St., Strand, London, W.C.2; John Wiley & Sons, Inc., 440 Fourth Ave., New York 16, 1951.

Intended for the use of research workers in the field of genetics, this book presupposes a thorough understanding of modern theories of inheritance as well as a secure grounding in calculus and mathematical statistics. The author takes up in turn a series of genetic problems in which computations of probability have to be made, beginning with comparatively simple ones from the field of inheritance in animals and going

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Thorax, London

6:103-208 (June) 1951

Effect of Posture on Diaphragmatic Movement and Vital Capacity in Normal Subjects with Note on Spirometry as Aid in Determining Radiological Chest Volumes. O. L. Wade and J. C. Gilson.—p. 103.
Experimental Asbestosis in Rats: Effect of Particle Size and of Added Alumina. J. M. Smith, I. D. P. Wootton and E. J. King.—p. 127.
Observations on Haemodynamics of Pulmonary and Lobar Atelectasis. J. C. Gilroy, V. H. Wilson and P. Marchand.—p. 137.
Intradiaphragmatic Mesothelial Cysts. G. Cruickshank and D. B. Cruickshank.—p. 145.
Possible Case of Oedematous Fibroma with Inflammatory Changes. V. Eskelund.—p. 154.
*Intrapleural Haemorrhage in Artificial Pneumothorax. J. T. Harold. —p. 162.
Agenesis of Lung. P. Wexels.—p. 171.
Fatal Acute Iodism After Bronchography. J. Sumner, A. I. Lichter and E. Nassau.—p. 193.

Intrapleural Hemorrhage in Artificial Pneumothorax.—Records of 37 cases with intrapleural hemorrhage of not less than one pint (473 ml.) developing after induction of artificial pneumothorax or after thoracoscopy are reported. The blood should be emptied early after it has entered the pleural space. The aim is to reduce foreign matter to a quantity that the pleura can absorb, and to reduce pleural exudate and so prevent secondary clotting. The first three days are vital, the risk of secondary clotting being reduced by aspiration during this period. Fragmented primary clot or secondary clotting may make further needle aspirations impossible. Thoracoscopic aspiration was performed in seven of nine patients with clotted hemothorax. If clot remains in the pleural cavity despite simple and thoracoscopic aspiration, thoracotomy and clot removal should be undertaken. This measure was used in only two of the 37 cases, and in both the artificial pneumothorax was lost. Before employing operative measures, the use of liquefying enzymes derived from hemolytic streptococci might be considered. They are streptokinase and streptodornase, the former liquefying fibrin and the latter nucleoprotein. When injected intrapleurally the enzymes cause liquefaction of the clotted hemothorax and a severe pleural effusion. A brief febrile reaction generally accompanies these changes, after which simple aspirations are again possible. If bleeding continues, attempts may be made to identify the bleeding point, but in the light of experience with thoracoscopy and thoracotomy carried out for this purpose, such attempts have little place in the early treatment of hemothorax complicating artificial pneumothorax. Decortication of clotted hemothorax is widely used in traumatic cases, but its use with artificial pneumothorax is not advisable, because preservation of the pneumothorax is desired for treatment of the tuberculous lung and because decortication will involve serious risk in patients with active pulmonary tuberculosis. The results obtained with different methods in these 37 cases suggest that simple aspiration is satisfactory. Deaths are rare, most patients do well, and a useful artificial pneumothorax usually remains.

Transactions Royal Soc. Trop. Med. and Hyg., London

44:611-764 (June) 1951. **Partial Index**

Recent Investigations into Treatment of Schistosomiasis by Miracil D in Egypt. J. Newsome.—p. 611.
Four Years' Experience of Sulphone Treatment of Leprosy. J. Lowe and T. F. Davey.—p. 635.
Biological Basis for Campaign Against Malaria Vectors of Brazil. M. Pinotti.—p. 663.
Strain of Monkey Malaria (Plasmodium Cynomolgi) Made Resistant to Proguanil (Paludrine). F. Hawking and J. P. Thurston.—p. 695.
Morphological Changes in Plasmodium Berghei Following Proguanil, Sulphadiazine and Mepacrine Therapy. J. P. Thurston.—p. 703.
Morphological Changes in Plasmodium Cynomolgi Following Proguanil, Sulphadiazine, and Mepacrine Therapy. J. A. McFadzean.—p. 707.
Studies on Protozoa—Part III.—Visceral Leishmaniasis in Cotton Rat (Sigmodon Hispidus). J. D. Fulton and J. S. F. Niven.—p. 717.
*Sickle-Cell Trait and Sickle-Cell Anaemia. H. Foy, A. Kondi and C. Alexandrides.—p. 729.

Sickle Cell Trait and Sickle Cell Anemia.—Foy and associates reason that if the sickle cell trait is regarded as a heterozygous condition (Ss) and sickle cell anemia as a homozygous state (SS), then sickle cell anemia can arise only as a result of the mating of two heterozygous persons (Ss x Ss), of a heterozygous and a homozygous (Ss x SS) person, or of two homozygous (SS x SS) persons. If this hypothesis is correct, then there should be more homozygous sickle cell anemia in a population with a high percentage of the trait than in a population with a low incidence of sickle cell trait. The prevalence of the sickle cell trait among certain of the Negro tribes of Africa, and the reputed absence of sickle cell anemia, means either that the present accepted genetic hypothesis is not entirely correct or that the anemia is far commoner than has so far been reported. Investigations so far carried out in Kenya show that owing to a high infant and/or intrauterine mortality rate in the homozygous, few survive to the age of puberty. If this work is confirmed, then sickle cell anemia should be found often in newborn babies and/or infants, and should be much rarer in adults. If this is the case, then death of the homozygous individual must be an important cause of infant mortality and may be a factor in the small families common in many African tribes. The authors discuss the case of a Greek girl who had sickle cell anemia, which contradicts the theory that sickle cell disease is evidence of Negro ancestry. Furthermore, only one of the patient's parents, the mother, had the sickle cell trait (Ss).

Ugeskrift for Laeger, Copenhagen

113:697-734 (May 31) 1951. **Partial Index**

*Precancerous Changes in Mucous Membrane of Portio; Examination of 104 Cases Observed for at Least Five Years. O. Petersen.—p. 697.
Outbreak of Food Poisoning Due to B. Cereus. O. Christiansen, S. O. Koch and P. Madelung.—p. 703.
Abacterial Meningitis with High Protein Content in Spinal Fluid. H. Letman.—p. 706.
Effect of Neptusan on Seasickness. V. Dyrberg and H. J. Laurtizen. —p. 710.
Raynaud's Disease Due to Protracted Use of Hypnotics? M. Matthiesen —p. 715.

Precancerous Changes in Mucous Membrane of Cervix.—Petersen states that in 104 cases with precancerous changes in the cervix (classified as leukoplakia simplex, leukoplakia with dedifferentiation, and leukoplakia observed for cancer) followed for five to 12 years, cancer developed in 14 (13.5%). In all groups the average age on the first examination in the Copenhagen radium station was 40.2 years. No cancer developed during the observation period in patients in the first group; cancer was found in six of the 30 patients in the second group after from 25 to 62 months, and in eight of the 24 in the third group after from five to 67 months. Control examinations of the changes in the mucous membrane of the cervix every three or four months, if feasible, are advised, especially in patients under 35. In or after the climacteric more radical interventions (total hysterectomy or radiotherapy) may be considered, but in these cases also the outlook for the patient will not, it is thought, be imperilled by a few months' expectant treatment with histological control. The histological picture of the epithelial changes afforded no indication as to possible later development of cancer.

113:773-810 (June 14) 1951. **Partial Index**

*Treatment of Whooping Cough with Chloramphenicol. L. C. Grandjean and H. C. A. Lassen.—p. 776.
Fracture of Body of Femur in Children. E. Naver.—p. 778.
Intussusception of Small Intestine Established on Roentgen Examination. T. Francis and M. Ottsen.—p. 785.

Chloramphenicol in Whooping Cough.—From the results in 100 proved cases of whooping cough treated with chloramphenicol Grandjean and Lassen conclude that this agent provides for the first time treatment for whooping cough effective in the great majority of cases. The treatment was followed by a sharp decrease in the attacks of coughing and by simultaneous notable improvement in the general condition. Chloramphenicol is regarded as indicated in all cases of whooping cough in infants and in graver cases in older children and adults. Determination of resistance of 45 whooping cough strains to chloramphenicol showed no resistant strain.

V 14
1951

BOOK REVIEWS

Handbook of Nutrition: A Symposium Prepared Under the Auspices of the Council on Foods and Nutrition of the American Medical Association. Second edition. Cloth. $4.50. Pp. 717, with 42 illustrations. Published for American Medical Association by Blakiston Company (Division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1951.

This edition of the Handbook of Nutrition is a symposium by some 30 leading authorities in the field of nutrition. Many of the articles were printed in THE JOURNAL during the preceding two years. The book is divided into four parts.

Part 1 is concerned with individual nutrients. The chapter on carbohydrate metabolism is especially well done. It points out that the catabolic pathways of the carbohydrates, fats, and proteins cross at many points and that within wide limits one nutrient may be substituted for another without significant injury to the metabolizing tissue. Each of the three major classes of nutrients may supply organic fragments that feed into the tricarboxylic acid cycle, a sequence of reactions that apparently serves to supply a large portion of the energy need of many biologic systems. As this fusion of metabolic pathways has been elucidated, the classic lines of demarcation between the metabolisms of fat, protein, and carbohydrate have become progressively more obscure and more meaningless. The picture that is developing is one of reaction sequences, often cyclic, that liberate energy as needed by the organism, and these cycles apparently may be fed at many points and in many ways. Part 2 concerns nutritional needs. The chapter on nutritional needs in illness and disease will be of interest to general practitioners. Part 3 deals with nutritional deficiencies. It contains unusually good chapters on caloric undernutrition and fluid therapy.

The last part of the book, on foods and their nutritional qualities, has an interesting and timely chapter on foods for emergencies. It points out that for populations in the path and in the wake of war, finding food becomes a matter of supreme importance. By utilizing edibles disregarded in normal times, much can be done to alleviate or postpone the worst effects of famine. Substantial contributions to the family larder can be made by gardening. By these means sufficient vitamins and minerals are usually obtainable. The pressing problems, then, relate to calories and biologically superior protein.

The Handbook has a reasonably good index. It is a useful addition to the literature of nutrition, a subject that is becoming increasingly recognized as of importance in medicine, both preventive and therapeutic.

Genetics in Ophthalmology. By Arnold Sorsby, Research Professor in Ophthalmology, Royal College of Surgeons, London. Cloth. $9.50. Pp. 265, with 233 illustrations. Butterworth & Co., Ltd., 4-6 Bell Yard, Temple Bar, London, W.C.2; C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

Arnold Sorsby is the author of numerous reports on a variety of ophthalmic subjects, all of great merit. He is also the editor of the important two volumes of "Recent Progress in Ophthalmology." His present contribution is his most important so far.

The subject of genetics is one in which few physicians have more than a passing interest, and very few ophthalmologists have sufficient background to properly interpret the frequent congenital and familial aberrations of the eyes encountered in their daily work. Sorsby is completely aware of this lack of knowledge and wisely, in a simple yet effective way, covers the facts and accepted theories of genetics in the first section of his book. The remainder of his work consists of a discussion of the ocular conditions known or suspected to be of genetic origin. Section 2 describes isolated anomalies occurring in every part of the eyeball and adnexa. Section 3 deals with the relation to ocular lesions of generalized disorders, e. g., metabolic and systemic disturbances, and with syndromes of ocular lesions.

Geneticists have long been aware of the important part that the eye has played in their science and have, along with many ophthalmogists, collected over the years, carefully and painstakingly, pedigrees of their patients. Sorsby has rendered a great service by gathering up these pedigrees from widespread sources and putting them into this relatively small and neat volume. In his preface he points out that the spotlight of medicine has shifted from infections, now for the most part under control, to the constitutional, environmental, and hereditary aspects of disease. "In some affections," he says, "the genetic factor is obvious. In others, it can be revealed only by exhaustive investigations aided by an understanding of genetic theory. The genetic anomalies have assumed greater significance with the recognition of modes of inheritance other than the simple autosomal recessives and dominants of the past. Isolated cases of genetic disease are no longer clinical puzzles and unusual modes of inheritance are more readily recognized."

The illustrations and charts are excellent, the book is beautifully printed, and the indexes are adequate.

Clinical Unipolar Electrocardiography. By Bernard S. Lipman, A.B., M.D., Assistant in Medicine, Emory University School of Medicine, Atlanta, Georgia, and Edward Massie, A.B., M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Missouri. Cloth. $5. Pp. 232, with 191 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1951.

This manual was developed from notes the authors used in teaching unipolar electrocardiography to the students of Washington University School of Medicine. Thus the material contained in this book has stood the test of the classroom. It is intended primarily for those who have had no experience in the subject, so that the presentation is elementary, concise, and at times dogmatic. Almost 200 diagrams and illustrations help to make clear a subject that is ordinarily complicated and difficult to understand.

Unipolar electrocardiography was introduced in 1933 by Frank N. Wilson and his associates. By connecting each of the three arm leads through a 5,000 ohm resistor to a central terminal, an indifferent electrode, which for all practical purposes has a potential of zero, was produced. Thus, the other electrode, known as the exploring electrode, can be placed anywhere on the body to record the electrical potential at that point. At first this technique was used as an important experimental tool, but now it has been shown to be of considerable clinical importance as well. For instance, unipolar electrocardiograms make it possible to determine fairly accurately the electrical position of the heart. The type of bundle branch block, the location of a myocardial infarct, and other electrocardiographic abnormalities are more clearly defined with this method than with the old bipolar, three-lead electrocardiogram.

This is not a textbook on electrocardiography, and such subjects as cardiac arrhythmias and vector electrocardiography will not be found in this book. The authors have limited themselves exclusively to unipolar electrocardiography. For those who are already familiar to some extent with clinical bipolar electrocardiography, this book will form an excellent introduction to unipolar electrocardiography.

The Measurement of Linkage in Heredity. By K. Mather, D.Sc., F.R.S., Professor of Genetics, University of Birmingham. Second edition. Cloth. $1.75. Pp. 149. Methuen & Co., Ltd., 36 Essex St., Strand, London, W.C.2; John Wiley & Sons, Inc., 440 Fourth Ave., New York 16, 1951.

Intended for the use of research workers in the field of genetics, this book presupposes a thorough understanding of modern theories of inheritance as well as a secure grounding in calculus and mathematical statistics. The author takes up in turn a series of genetic problems in which computations of probability have to be made, beginning with comparatively simple ones from the field of inheritance in animals and going

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

on to some difficult problems of human inheritance. The latter include the ABO factors in blood (page 131), the MN factor (page 127), and the ability to taste phenylthiocarbamide (page 125). The author deserves praise for the pains he has taken to be clear and explicit, and the general plan of the book, that of taking up each problem as a unit and giving its numerical solution in detail, is excellent. The book will be invaluable to anyone engaged in genetic studies.

Treatment of the Nephrotic Syndrome. By Lee E. Farr, M.D., Chairman, Medical Department, Brookhaven National Laboratory, Upton, Long Island, New York. Publication number 64, American Lecture Series, monograph in American Lectures in Circulation, edited by Irvine H. Page and Arthur Curtis Corcoran. Cloth, $1.75. Pp. 61. Charles C Thomas, 301-327 East Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1951.

In this small volume, the author summarizes his views on the treatment of the various symptoms that accompany the nephrotic syndrome. Dr. Farr has had extensive clinical and investigative experience with children with nephrosis, and in this review he submits his own appraisal of the myriad forms of treatment that have been used over the years since nephrosis was first described by Muller and later by Funk and by Volhard and Fahr.

The author defines the nephrotic syndrome as a clinical term used to describe a disease complex characterized by edema, hypoproteinemia, lipemia, and proteinuria, with doubly refractile bodies in the urine and generally without hypertension or severe cardiac failure. It is in this sense that the term is at present generally used among pediatricians and includes what was formerly called pure nephrosis and also the nephrotic stage of chronic glomerulonephritis.

The first and longest chapter deals with the treatment of edema. The one common measure used by all who treat the nephrotic syndrome is a low sodium diet. It is generally agreed that the sodium in the diet should be kept down to 400 to 600 mg. per day; this can be done now that salt-free milk is available. The author does not advise any specific diet aside from the low salt diet. His results with serum, plasma, and albumin have been disappointing. He does not advise diuretics except urea; he suggests that there should be a trial of the latter in every edematous patient.

Chapters follow on treatment of malnutrition, renal failure, and complications. Penicillin is still considered to be the drug of choice in treatment of the many acute infections that complicate the nephrotic syndrome. A final chapter on treatment discusses the newer agents: corticotropin (ACTH), cortisone, and nitrogen mustard. He concludes that at present there is not enough evidence to justify the use of these dangerous agents except under the most careful hospital observation. Even then complete recovery cannot be expected, but there may be relief of edema. A final short chapter gives excellent advice on the treatment of the patient as a person.

Physiotherapy in Obstetrics and Gynæcology (Including Education for Childbirth). By Helen Heardman, M.C.S.P. With forewords by W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G., Professor of Obstetrics, University of London, and Veronica Shand, S.R.N., S.C.M., M.T.D., Supervisor of Midwives, Lancashire County Council. Cloth. $3.50. Pp. 498, with 94 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1951.

One hesitates to criticize this book too severely, because in his foreword Dr. Nixon mentions that Mrs. Heardman, the author, was killed in a motor accident shortly after handing the manuscript to her publishers; nevertheless it would seem that the author was hardly qualified to discuss the more complicated phases of obstetrics and gynecology and that it would have been better for one of the specialists in physical medicine at the University College Hospital, where she worked, to prepare this text. This monograph is divided into three parts: part one, on the female reproductive function, includes the anatomy of the reproductive system and also the physiology and psychology of reproduction; part two deals with physiotherapy in obstetrics (including education for childbirth); and part three deals with physiotherapy in gynecology.

The author is an advocate of the controversial writings of Dr. Grantly Dick Read on "natural childbirth" and recommends that readers study Dr. Read's "Childbirth Without Fear." To begin with, the book is based on an erroneous major premise, which is that childbirth is attended by pain, fear, and tension, and that if pain is eliminated fear and tension remain; whereas if fear is eliminated "pain and tension will not appear (because there is no cause for them)." This premise is not correct, because it is not true that the process of childbirth is painless simply because the patient is not in fear of pain. Also, the importance of "physiotherapy" as related to obstetrics and gynecology is obviously overstressed. Nevertheless, there are many interesting observations and helpful recommendations. The book is well printed, well illustrated, and fairly well documented. Exercises to prepare the patient for labor, procedures to prepare the patient for lactation, and postnatal exercises are carefully described, with suitable illustrations. The section on gynecology is incomplete and not too satisfactory. This textbook will be of some interest to physicians specializing in physical medicine, but can hardly be recommended as a guide for physical therapists until the whole subject is better clarified.

From a Doctor's Heart. By Eugene F. Snyder, M.D. With foreword by Paul Dudley White, M.D. Cloth. $3.75. Pp. 251, with illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

After years of trying situations and caring for other people's ills, the doctor, his wife, and his son took a vacation. Before arriving at their destination, the doctor had a painful coronary occlusion. The rest of the book is the physician's point of view toward heart disease when the patient happens to be the physician.

Dr. Snyder spent the early years of his life in Russia; he took professional training in Czechoslovakia after fleeing from the Bolshevists and then became established in the United States after fleeing from the Nazis. Throughout his book the attitudes toward life, death, and illness are richly flavored by the philosophy of one who had suffered many trying situations, has known fear, and yet has found his place in the world. A physician might do well to give this book to a patient recovering from heart disease or one who is destined to be a heart victim in the future. The psychosomatic aspects of medicine and the problems that are faced by the victim of heart disease are clearly set forth as the doctor explains to his teen-aged son the meaning of his hospitalization and the adjustments that must be made. The advice and observation of an old general practitioner who survived his coronary attack by 25 years adds much that would be helpful to those who do not know the true attitudes of the physician. This is a stimulating volume, touching on philosophy, psychology, and medicine with enough of the spiritual to give it the right flavor.

Tropical Nutrition and Dietetics. By Lucius Nicholls, C.M.G., M.D., B.C. Third edition. Cloth. $6; 42s. Pp. 476, with 74 illustrations. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, Maryland; Baillière, Tindall & Cox, 7-8 Henrietta St., Covent Garden, London, W.C.2, 1951.

This is a well-revised, useful presentation of medical nutrition and dietetics as related to tropical areas. The remarkable integration of basic information and practical approach to tropical nutrition reflects the author's personal contact and long interest in nutrition in Ceylon.

The author has succeeded admirably in providing a readable, concise account of the general principles of nutrition and dietetics which should be of value and interest to physicians, students, nutritionists, and social workers who have responsibilities in tropical or semitropical regions. In addition, similar categories of workers in temperate climates will find the first 235 pages of the book (chapters discussing the principles of nutrition, disorders of malnutrition, processing and preparation of food, and classification of foodstuffs) of real value. The remainder of the book will be of interest to many workers in the temperate regions because it provides a description of a large variety of foodstuffs which are important in the tropics but which are often unfamiliar to workers in other areas.

The section on food poisoning provides a valuable summary of the ill effects that result from substances naturally present in certain common as well as exotic foods. Particularly to be commended is the section on public health activities in relation to

V 14
1951

nutrition. This deals with dietary surveys, nutritional surveys, and the practical application of nutritional knowledge.

This book is deserving of wide reading by workers in tropical regions, in underdeveloped countries generally, and persons with an interest in nutrition and foods in temperate regions.

Speech Habilitation in Cerebral Palsy. By Marion T. Cass. Cloth. $3. Pp. 212. Columbia University Press, 2960 Broadway, New York 27; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1951.

One of the most distressing aspects of cerebral palsy is the difficulty an otherwise intelligent patient may have in communicating ideas or even hinting at his feelings. Hence, great interest attaches to recent efforts to apply the gradually developing science of logopedics or phoniatry to such patients. This work deserves the highest praise. After a summary of relevant facts on the etiology of cerebral palsy and the neuroanatomic basis of the associated speech difficulties, the author gives a systematic and detailed account of the procedure for improving the speech. A concluding chapter discusses other educational problems and suggests additional rehabilitative measures. The book will be valuable to speech therapists but should be perused by every general practitioner who is called on to deal with a case of cerebral palsy.

Modern Dietetics. By Doris Johnson, B.S., M.S. Edited by Hazel E. Munsell, Ph.D. Cloth. $4.95. Pp. 529. G. P. Putnam's Sons, 210 Madison Ave., New York, 1951.

This book is written especially for the student nurse but should prove interesting and useful for many in the medical profession. In it will be found accurate answers to questions patients need to have answered about foods and cookery. The author has had a wide experience in hospital dietetics and the teaching of the subject. She is fortunate in having the expert guidance of Dr. Munsell in the preparation of her material.

The first section of the book deals with the basic normal daily dietary pattern. Part 2 indicates how the normal diet is modified to meet therapeutic requirements. Part 3 deals with cookery. Part 4 is made up of various tables that are necessary tools in the practice of dietetics. One way a physician can keep his patients away from food faddists is to have a textbook like this available for frequent and easy reference.

Your Health. By Dean Franklin Smiley, A.B., M.D., Secretary of Association of American Medical Colleges, Chicago, and Adrian Gordon Gould, Ph.B., M.D. Cloth. $4.50. Pp. 555, with 137 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

The authors have added to their previous successful books, "Personal and Community Hygiene" and "A College Textbook of Hygiene," this book, which is also intended for college students and which replaces the latter book under a new title. It is a soundly documented textbook like its predecessor. It is broad and comprehensive in scope, popular in treatment, readable in style, attractive in format, and clear in exposition. It is liberally illustrated, with a wide variety of illustrations ranging from pictographs to photographs. The preventive medicine and public health viewpoint is emphasized. It is a sensible, practical, reliable, and thoroughly useful contribution to its field and can be heartily recommended.

Therapeutics in Internal Medicine. Edited by Franklin A. Kyser, M.D., M.S., F.A.C.P., Associate in Medicine, Northwestern University Medical School, Chicago. Cloth. $7.50. Pp. 715. Thos. Nelson & Sons, 19 E. 47th St., New York 17; Parkside Works, Dalkeith Road, Edinburgh 9, Toronto, 1950.

The therapeutics of 1951 is difficult to encompass, either in a single volume or by a single author. Dr. Kayser, in his preface, states that he thinks the latter is now almost an impossibility, but he and his many authors have accomplished the first very satisfactorily. They have written a readable and adequately detailed description of the treatment of almost all the conditions encountered in the practice of internal medicine. The contributors are largely from Chicago and the Middle West and include many distinguished medical names.

Present day books on therapeutics fall largely into the class of larger volumes like this one, which are likely to be left at home or in the office, and small manuals or handbooks which may be carried easily. Both types seem to serve useful purposes; of the larger type this one by Dr. Kayser appeals somewhat more than some, possibly because the presentations have a slightly contemplative, instead of staccato, air.

Books, and even articles, in these days are often out-of-date almost before they appear. The publishers must have done very well with this book, for the signs of delay are largely missing. The new antibiotics and cortisone are well covered, but troubles with potassium a little less so.

The book is recommended as a reliable guide to treatment; it is well organized and well printed. As minor criticism, the occasional preference for the apothecary system, and for preparations not mentioned in New and Nonofficial Remedies or official volumes, is noted.

Manual of Massage and Movements. By Edith M. Prosser, T.M.M.G. Cloth. $5. Pp. 388, with 287 illustrations by M. Ruddick. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1951.

This is a thoroughgoing and well-illustrated textbook on massage and exercise by an "Examiner for the Chartered Society of Physiotherapy" of England. The author has attempted to present the subject in an interesting fashion and has illustrated the book profusely with drawings of "match figures." The book begins with a discussion of massage, continues with a detailed description of various therapeutic exercises for different parts of the body, and closes with a discussion of the use of therapeutic exercise in the management of various spinal deformities. Because of its thorough coverage of the subject and because of its many illustrations, it is a valuable text for the physical therapist and will be of much interest to physicians concerned with physical medicine.

The Modern Woman's Medical Guide. Edited by Aaron H. Horland, B.S., M.D., and Charles S. Steinberg, A.B., M.A. With foreword by R. B. Robins, M.D., Past Vice-President, American Medical Association. Cloth. $3.50. Pp. 393. World Publishing Company, 2231 W. 110th St., Cleveland 2, Ohio, 1951.

This book is a compilation of articles reprinted from many sources, including books, pamphlets, and journals. As indicated in the title, this book deals specifically with women's problems —marriage, pregnancy, planned parenthood, advice for mothers of young babies, care of the skin and hair, information on sex problems of the adolescent, and material on the menopause as well as miscellaneous topics such as bachache, allergies, headaches, fatigue, weight control, and cancer. The material selected is by competent and reputable authors. In a few instances, the editors have furnished short articles to round out the scope of the book. It can confidently be recommended to patients.

Atlas der Hals-,Nasen-,Ohrenkrankheiten: Eine Sammlung typischer Krankheitsbilder mit topographischen, diagnotishen und therapeutischen Hinweisen. Von Carl von Eicken, und A. Schulz van Treeck. Third edition. Cloth. 78 marks. Pp. 199, with 470 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O.: agents for U. S. A., Grune & Stratton, Inc., 381 4th Ave., New York 16, 1951.

It is pleasant and rewarding to turn the pages of this atlas, to observe the artistry that went into the figures, to be aware of the erudition and high standards of that school of medicine which, once the pride of the world, today is no longer in the forefront.

Those portions which deal with anatomy can hardly be improved; it is in the sections that discuss disease and therapy that one senses how far German medicine of today has regressed. For example, there are pictured fully developed conditions that American antibiotic therapy does not permit to develop. Many of these conditions, in this country at least, may be said to have become, in a practical sense, so modified in character or so seldom seen as to be nonexistent. This would apply especially to the acute bacterial diseases of the pharynx, larynx, and ear, and especially to the severe and often fatal complications of these conditions. Today a medical student sees these no more than he sees typhoid or diphtheria.

It is this which gives this book a slightly unreal and old-fashioned aspect, but by no means reduces in value the large amount of interesting material that still remains.

QUERIES AND MINOR NOTES

INJECTIONS DURING POLIOMYELITIS SEASON

TO THE EDITOR:—*We have had a number of inquiries from patients as to the validity of a newspaper editorial that warned against the administration of injections during the poliomyelitis season. Since our practice is limited to allergy, injections are necessarily a major feature of our approach. What is the opinion of authorities as to administration of hyposensitization or other injections during the poliomyelitis season?*

Clifford H. Kalb, M.D., Milwaukee, Wis.

ANSWER.—The editorial to which reference is made was the outgrowth of a series of communications, some of which are noted herewith: J. K. Martin (*Arch. Dis. Child.* **25**:1 [March] 1950) presented a series of 17 children under three years of age, in whom paralysis of a limb followed injections of pertussis vaccine, APT and TAF and penicillin. These were selected cases and did not indicate the frequency of such paralyses in comparison with cases in which injections had not been given. B. P. McCloskey (*Lancet* **1**:659 [April 8] 1950) reported a study of 375 patients with poliomyelitis in Victoria in 1949, of whom 340 were investigated. Of these, 31 children had been inoculated three months or more recently with pertussis vaccine, diphtheria toxoid, or a combination of the two. Thirty of these 31 had paralysis. The paper does not disclose the incidence of paralysis in the entire series of cases. In six patients, nine limbs inoculated with pertussis vaccine became paralyzed and two did not. Of the uninoculated limbs, three became paralyzed and 10 did not. In 14 patients receiving combined pertussis vaccine and diphtheria toxoid, 18 inoculated limbs became paralyzed and three did not. Of the uninoculated limbs, seven became paralyzed and 28 did not. In 10 patients receiving diphtheria toxoid, six inoculated limbs became paralyzed, while seven did not. Of uninoculated limbs, eight became paralyzed and 13 did not. The following significant figures were presented by the author: Of 15 children inoculated less than 35 days before poliomyelitis developed, there were 16 paralyzed limbs; in 48 children in the control group, there were 62 paralyzed limbs. It is obvious that these data do not present a clean-cut indictment of these inoculations with respect to the development of paralysis, although they do point to the possibility that inoculations might determine localization.

An editorial in THE JOURNAL (**144**:240 [Sept. 16] 1950) pointed out the essence of these and similar reports but cautioned against the complete acceptance of the idea that such inoculations cause paralysis. Early in the summer there was a great deal of sensational newspaper publicity regarding this topic, and there was great distortion of some of the known facts. There followed a ruling by the New York health department regarding inoculations. After this confusion the New York *Times* printed an article that clarified some of these points: "The Council (Coordinating Council of the Medical Societies of the Bronx, Kings, New York, Queens and Richmond) emphasized that the ruling by the Health Department was never intended to apply to injections that have immediate therapeutic usefulness, including antibiotics like penicillin, gamma globulin, tetanus and diphtheria antitoxin, or antirabies and typhoid vaccines. Nor was the ruling intended to apply to smallpox vaccinations or injections for allergies.

"Dr. McCarty (Secretary of the Council) said the confusion among the public seemed to have arisen from the fact that some persons seemed to believe the statement said that injections would cause infantile paralysis. No such statement was ever made. Injections per se do not cause infantile paralysis, the Council emphasized."

R. S. Patterson (*Am. J. Pub. Health Rep.* **41**:875 [July] 1951) states: "Some British health people have been concerned about possible relationships between site of immunization and subsequent polio involvement. In a recent Belfast experience, no association was found, but it will take many more than a single negative observation to kill that concept—loaded as it is with obstacles to diphtheria control."

The whole subject may be summarized as follows: It is possible, though not proved, that localization of paralysis may be influenced by injections of pertussis vaccine or diphtheria toxoid. There is no clear evidence that it influences the incidence of paralysis. There is no suspicion that any of these inoculations favors the incidence of poliomyelitis. As regards the question of antigens used in desensitization (pollen, dust) there has been no claim that they have any effect whatever on the onset or course of poliomyelitis. As a matter of fact, in a follow-up of thousands of patients receiving desensitization therapy, there was no suspicion of any association of these injections with the incidence of poliomyelitis, the incidence of paralysis, or the localization of the paralysis.

BOWEL DISTURBANCE AND DIABETES

TO THE EDITOR:—*A man, 52, on Jan. 27, 1950, had massive gastrointestinal bleeding from a duodenal ulcer; then he was relatively well until October, when diarrhea developed, with four to five soft, watery, green stools per day. Results of a sigmoidoscopic examination on Oct. 30, 1950 (distance of 20 cm.) were negative. Stool examinations and barium enema disclosed no abnormalities. The patient has had diabetes since 1941. Because there appeared to be no roentgen or laboratory evidence of significance, he was given diiodohydroxyquinoline as a therapeutic trial, without significant improvement. He was referred to an internist, who repeated the above studies and found nothing of importance. However, because of the past history of diabetes, which apparently is well controlled, it was suggested that vitamin B_{12} be given. The patient has been receiving 30 mg. of vitamin B_{12} for eight weeks, without response. Kindly suggest further diagnostic studies or therapeutic trials.*

M.D., California.

ANSWER.—This patient's problem is not uncommon, and in this situation the question always arises as to whether the bowel disturbance is related to the diabetes. Careful and repeated examinations of the stools must be made to rule out bacterial and parasitic causes. As has already been done in this case, sigmoidoscopic examinations and roentgen studies of the gastrointestinal tract must be done to establish disease apart from diabetes, if such exists. "Irritable bowel," mucous colitis, and early stages of ulcerative colitis must be considered. Even if results of studies have been negative, they should be repeated, at least in part, after some weeks or months if the condition persists.

Assuming that conditions apart from diabetes have been ruled out, then it is safe to assume that the diarrhea may be a manifestation of "diabetic neuropathy." In such patients, there will usually be coexisting peripheral neuritis or a past history of such. Furthermore, the history will indicate a period of relatively poor control of diabetes either in the recent or more distant past. Examination of the spinal fluid will characteristically reveal an increase in the total protein without the presence of cells. "Diabetic diarrhea" often is chiefly nocturnal, and not infrequently nocturnal incontinence of feces occurs. It is characterized by remissions and relapses. Treatment is in general unsatisfactory, but in many cases the tendency to diarrhea gradually subsides, particularly if the diabetic condition is kept under careful control. A low residue, nonirritating diet, with body relaxation before and after meals together with restriction of liquids at meal times, may be helpful, as in any diarrhea. Vitamin supplements, particularly of vitamin B, often appear to be

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

V 14
1951

beneficial, though not dramatically so. Certain clinicians have thought that administration of crude liver extract intramuscularly over a period of weeks or months is effective. Despite favorable reports of some workers, others have found no significant benefit from vitamin B_{12}.

GONORRHEA

TO THE EDITOR:—*A woman, 39, married, had contracted gonorrhea in 1933 and probably had salpingitis and pelvic peritonitis at that time. For 10 years she kept having a small amount of yellowish discharge, which ceased entirely in 1943. Numerous smears were negative and I assured her that she was cured. In July, 1947, she was hospitalized for a sinus infection. For seven days she was given 50,000 units of penicillin sodium every three hours and 1.0 gm. of sulfadiazine every four hours. She did not have any pelvic symptoms until one month ago, when she suddenly had severe pain in the left side of the pelvis, which gradually spread to the right side. There was moderate rigidity and temperature of 101 F. Cervix had a normal appearance. The cervical plug was tenacious. A smear showed few pus cells and no intracellular organisms. However, the culture was positive for gonococci. The patient denies extramarital relations. The husband had gonorrhea 20 years ago, but no signs of disease since then. Prostatic smear and culture were negative. The patient improved after two weeks of intensive chemotherapy and treatment with penicillin, streptomycin, and aureomycin. Was I wrong in assuring the patient in 1947 that she was cured? Is it a frequent occurrence for a gonorrheal infection to flare up after being dormant for 18 years? Can I assure her now that she is cured? Is a salpingectomy indicated in this patient?*

M.D., Colorado.

ANSWER.—It is not possible to answer positively the questions raised in connection with this case. More information might have been obtained if the marital partner had been subjected to complete physical and bacteriological examinations in 1947 and when the patient's pelvic infection recently complicated the picture. A gonococcic infection of 18 years' duration is rare, although such cases have been reported. Probably, therefore, the patient did not have the original gonococcic infection in 1947.

Determination as to whether gonorrhea exists at present should be based on careful examination of the marital partner as well as bacteriologic examinations of the patient during two or three successive postmenstrual periods. These examinations should include a culture on each occasion. Every advantage should be taken of the utilization of the antibiotics in the treatment of this patient before a salpingectomy is done. If the subjective symptoms of pelvic disease continue, after the process becomes chronic, a salpingectomy might be indicated.

DISTRESSING GAS DURING PREGNANCY

TO THE EDITOR:—*What relief might be given to a white 33 year old woman (gravida 3) who complains of distressing abdominal "gas" which begins about 4 p. m. and is most distressing from 8 p. m. until early morning. The only other symptom is occasional slight nausea. The first born was a footling, with resultant fatal injuries during vaginal delivery. No gas was noted during this pregnancy. The second pregnancy terminated with cesarian section after 28 weeks because of premature labor, again with footling presentation. The patient is now two months pregnant and has complained of similar distressing gas, which prevents sleep. Medications given without success include intravenously administered pyridoxine hydrochloride, several aluminum hydroxide preparations, dilute hydrochloric acid, activated charcoal, belladonna tincture and mild sedatives. Diet seems to have no influence. The patient's bowels move daily with caroid* and bile salts every second evening.*

Joseph L. Eckenrode, M.D., Lancaster, Pa.

ANSWER.—This patient has had almost all the medication that might help to relieve gas. Unfortunately there is no specific remedy for this distressing condition. The best that can be done is to alternate different mild remedies until the symptom disappears spontaneously, which it will do.

INFECTION IN URINARY TRACT

TO THE EDITOR:—*A diabetic, 31, requiring 60 units of protamine zinc insulin supplemented by 5 to 20 units of regular insulin was seen Oct. 7, 1950, with rather heavy pyuria, blood pressure 180/90, bacteria in freshly voided urine (testing both glasses). He also showed Bacillus lactis organisms which appeared to clear up with terramycin therapy. Insulin requirements were reduced to 25 units of NPH insulin. The source of infection seemed to be the prostate. Prostatic massage was instituted, edema largely cleared, and blood pressure came down, but in a month's time, the patient had a relapse, with hypertension and a nephritic type of edema. Pyelograms were normal. Gantrisin,* terramycin, chloramphenicol, and aureomycin, as well as calcium mandelate, were tried, without any clearing of the infection. Cultures of the urine now show Proteus rettgeri. Sensitivity tests using the sulfonamides and all the commonly available antibiotics showed no inhibition of growth. Any advice would be appreciated.*

Alfred B. Sundquist, M.D., Manchester, Conn.

ANSWER.—It is difficult to determine the source of infection in the urinary tract from the clinical data that have been submitted. Although prostatitis can be the only source of urinary infection, this is not usually the case. It will be necessary to exclude the kidneys, ureter, and bladder as sources of infection by means of roentgenographic, urographic, and cystoscopic studies. Elimination of these sources of infection would be fully as important as your identification of the etiological type of bacteria. Prostatic infection alone seldom causes hypertension or the edema that you refer to. There must be other causes involved. The improvement in clinical observations as a result of prostatic massage is probably only coincidental. An authoritative review should be made of the diabetic status in this case as well as its therapy. It is well known that urinary infection in the diabetic patient often is persistent despite the usual forms of antibacterial treatment. In regard to the choice of antibiotics, Bacterium aerogenes usually responds rapidly to aureomycin. The results of recent cultures showing the presence of a proteus is rather unusual. It is not stated whether the Proteus in this case has urea-splitting qualities. If patients with Proteus infection do not respond to one of the sulfonamides, adequate dosage with aureomycin should be employed.

PRURITUS FOLLOWING HERPES ZOSTER

TO THE EDITOR:—*A patient with paresthesia of the face following herpes zoster ophthalmicus was treated with chloramphenicol and recovered, i. e., the skin lesions dried and healed completely after two weeks, but intolerable pruritus persists even after three months. What is the prognosis?*

M.D., New Jersey.

ANSWER.—The treatment of post-zoster pain or pruritus is not too satisfactory. Fortunately, in most cases there is gradual improvement until, finally, all discomfort ceases. Heat—both superficial and deep—x-ray therapy, the administration of sedatives, the application of bland creams containing antipruritic agents, as 0.1% menthol, the intravenous administration of sodium iodide, and the use of protamide* (colloidal solution of processed and denatured proteolytic enzyme for intramuscular injection) all have their advocates.

COLOR OF CHILD OF MIXED PARENTAGE

TO THE EDITOR:—*If a light yellow Negro marries a white woman, is it possible, or probable, for them to have a child darker than the father?*

M.D., New York.

ANSWER.—A study made in Bermuda of crosses between white spouses and light-colored spouses (presumably with one genetic factor for pigmentation, when four factors represent the full-blooded Negro) showed that 22 such matings produced 56 children of the same grade of color as the white parents, 80 children of the same grade of color as the colored parents, and one child somewhat darker than the colored parent. Thus the chance of the child of a white woman and a light yellow Negro man being darker than the father appears to be about one in 137.

RECURRENT DEPRESSIONS

To the Editor:—*A man, 49, up to three years ago enjoyed excellent health. At present his health is good and his examination gives normal results. Three years ago, he began to notice that he was getting tired, lost his pep, his mental acuity diminished, usual business activities and decisions that he ordinarily did not give a second thought to became major problems. He had no desire to talk to others, and he became pessimistic. Six weeks later he suddenly became normal again. He describes it as if a cloud had lifted from his mind. The second spell appeared in 1949. This one had the same gradual beginning, lasted about three months, and then disappeared. His physical examination was again negative. However, he felt like crying at times, had no desire to live, and shunned all social contacts. I have tried giving dexedrine,® testosterone by injection, and metandren® sublingually, but none of those seem to help. What can be done to prevent the recurrence of these spells? His personal life has been happy. The only disappointment that could contribute to this state is that he is somewhat disappointed in the personality of his eldest son, who is a junior in a school of engineering.*

M.D., Missouri.

Answer.—This patient has recurrent depressions, probably involutional in character or manic-depressive in type. He may have had previous depressions that he fails to recall. He probably does not have organic disease of the nervous system, in view of the complete absence of symptoms between episodes of depression. Medication will probably not prevent recurrence of his depressions, unless there is some unrecognized organic factor of which the depression is a symptom. If there is no neurological disease, the only means of preventing recurrence is psychiatric treatment. It is not possible to promise control of his episodes by such treatment, but it offers the best possibility of doing so. For evaluation of his problem, he should be seen by a psychiatrist, who can then determine whether treatment is advisable and whether prevention of future attacks is possible.

FLEETING PAINS, EPISTAXIS AND SPITTING

To the Editor:—*Two years ago my daughter, who is now almost 8, began to complain of abdominal pains, fleeting in nature, and frequent nosebleeds consisting of a slight ooze. Physical examination disclosed no abnormalities. There were no cardiac murmurs; the white blood cell count and the sedimentation rate were normal. Because of previous episodes of tonsillitis, tonsillectomy was performed. After that the complaints ceased for two years and then began again. The pains were fleeting but occurred many times a day. At the same time she began to spit a lot, especially in her own home. No physical abnormalities were observed, and the white blood cell count and the sedimentation rate were normal. She spent March and April, 1951, in Florida, and the complaints ceased except for occasional pains in the limbs and chest and abdomen (not joints). Since returning to New York City, she has again begun to complain of frequent aches and pains. I would appreciate advice as to diagnosis and treatment.*

M.D., New York.

Answer.—In view of the negative results of the physical examinations and laboratory studies, together with the cessation of complaints for two years following tonsillectomy, and for the two months in Florida, when the child was away from home, one would be led to suspect a psychological, rather than a physical, basis for the symptoms described. It would be well to inquire into the child's environment, both at home and at school. Are there siblings who annoy or torment her? Are there other members in the household who too severely discipline or inhibit her normal desires? Is the teacher at school too strict or severe. Or, are there school playmates who tease or torment or otherwise upset her? Is she having difficulties with her school work; if so what is this difficulty? Does she suffer from strephosymbolia? All phases of the child's life, environment and associates, should be investigated in search for a psychic maladjustment that might explain the symptoms herein detailed. If this search is unsuccessful, it might be well to consult a child psychiatrist.

THROMBOPENIC PURPURA

To the Editor:—*A child has thrombopenic purpura with hemorrhages of intestinal origin and very low blood thrombocyte count. Microscopic examination of the bone marrow disclosed, besides pronounced aplastic phenomena, an absence of megakaryocytes. The treatment has been based on transfusion, and the thrombocyte count always rises above 200,000. Some members of our staff believe that splenectomy may help in this case, while others consider it contraindicated. For this reason we decided to ask for your advice.*

A. P. Gavilan, M.D., Durango, Mexico.

Answer.—The data supplied are insufficient to permit a diagnosis. One would like to know whether the patient has anemia (unrelated to blood loss) and whether there is leukopenia besides the thrombopenia. Is there splenomegaly? Are there developmental defects associated with the hematologic abnormalities as they occur in the so-called Fanconi syndrome? (See Estren, S.; Suess, J. F., and Dameshek, W.: *Blood* **2**:85 [Jan.] 1947.) To ascertain whether there really is no hypoplasia of the marrow, a surgical biopsy may be indicated. If no megakaryocytes are found in the marrow, it is unlikely that splenectomy will give beneficial results. Some of these hypoplastic myelopathies respond to prolonged treatment with cortisone or corticotropin (ACTH).

VENOUS PUNCTURE IN INFANTS

To the Editor:—*We frequently require about 8 cc. of blood to perform certain tests on infants and young children. Either venous or arterial blood is acceptable. The antecubital and scalp vein approaches often prove unsatisfactory, and we have been unable to find adequate descriptions of other avenues of approach. What other techniques can be expected to yield this quantity of blood without excessive hazard?*

M.D., West Virginia.

Answer.—Besides the arm and scalp vein approaches for withdrawing blood from infants and young children, those familiar with the technique have successfully used the ankle and external jugular veins in withdrawing blood for laboratory tests. The deeper veins and arteries, such as the femoral arteries or veins, the carotid artery, or internal jugular vein, yield blood if skilfully punctured, but fatal hemorrhage has been reported from puncture of these deep arteries and veins, and they cannot be recommended as safe sites for the withdrawing of routine blood samples. The longitudinal sinus should never be used as a site for withdrawing blood from infants, even though the anterior fontanel is open. The application of a warm, wet towel over a vein site often facilitates venous puncture.

EPIDERMOLYSIS BULLOSA

To the Editor:—*In a family with three children, the first was a normal male, now about 4 years old; the second, a boy born about two years ago, had epidermolysis bullosa and died at the age of 3 months; the third, a girl born Feb. 16, 1951, also has epidermolysis bullosa, but it apparently is not as severe as it was in the second child. The family history for any significant hereditary conditions is apparently negative. Can you tell me of any treatment and of the possibility of future children, if any, having this condition?* *M.D., New York.*

Answer.—There is no specific treatment for epidermolysis bullosa, and the possibility of its appearing in children to be born in the future cannot be predicted.

BLEBS FOLLOWING IRIDENCLEISIS

To the Editor:—*A patient had an iridencleisis performed four months ago. The tension is 22, but she has two elevated, slate-colored blebs above the limbus. What is the cause, and what should be done? She recently arrived in the country from England.* *M.D., Michigan.*

Answer.—The cause of the blebs following iridencleisis is a filtrating scar. The bleb is similar to that following trephine in a moderate proportion of cases. There is nothing to be done for it. It is advisable that the conjunctival sacs be kept as clean as possible by the regular use of a mild collyrium, such as 0.2 per cent zinc sulfate, twice daily.

V 14
1951